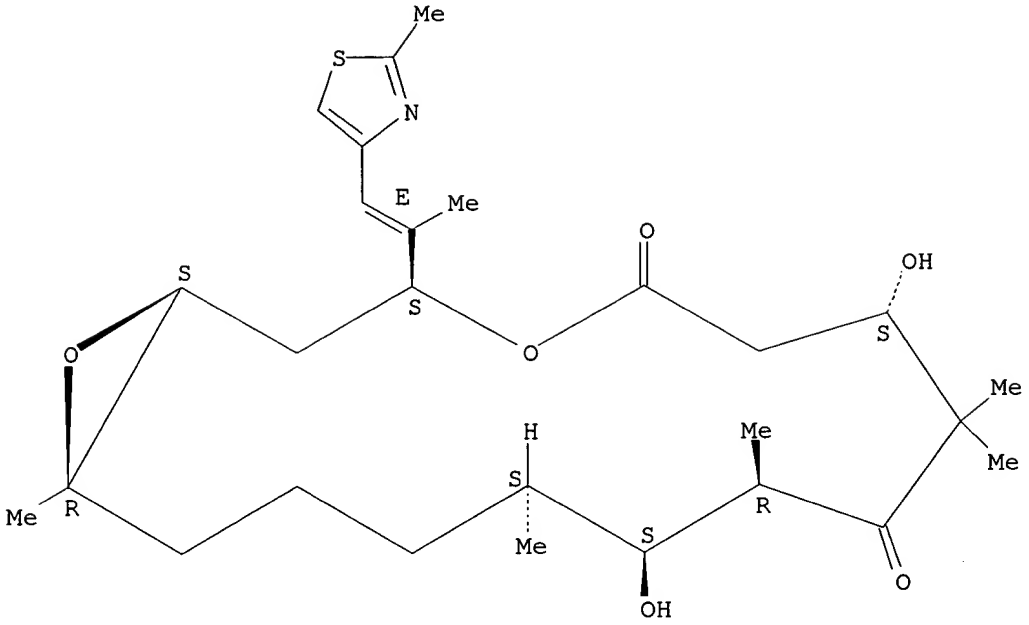
C-A-S. 8/27/01

=> d bib abs hitstr 1-207

L4 ANSWER 1 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 2001:425492 CAPLUS
TI Microtubule Structure at Improved Resolution
AU Meurer-Grob, Patricia; Kasparian, Jerome; Wade, Richard H.
CS Institut de Biologie Structurale, CEA/CNRS, Grenoble, 38027, Fr.
SO Biochemistry (2001), 40(27), 8000-8008
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Microtubule architecture can vary with eukaryotic species, with different cell types, and with the presence of stabilizing agents. For in vitro assembled microtubules, the av. no. of protofilaments is reduced by the presence of sarcodictyin A, epothilone B, and eleutherobin (similarly to taxol) but increased by taxotere. Assembly with a slowly hydrolyzable GTP analog GMPCPP is known to give 96% 14 protofilament microtubules. We have used electron cryomicroscopy and helical reconstruction techniques to obtain three-dimensional maps of taxotere and GMPCPP microtubules incorporating data to 14 .ANG. resoln. The dimer packing within the microtubule wall is examd. by docking the tubulin crystal structure into these improved microtubule maps. The docked tubulin and simulated images calcd. from "at. resoln." microtubule models show tubulin heterodimers are aligned head to tail along the protofilaments with the .beta. subunit capping the microtubule plus end. The relative positions of tubulin dimers in neighboring protofilaments are the same for both types of microtubule, confirming that conserved lateral interactions between tubulin subunits are responsible for the surface lattice accommodation obsd. for different microtubule architectures. Microtubules with unconventional protofilament nos. that exist in vivo are likely to have the same surface lattice organizations found in vitro. A curved "GDP" tubulin conformation induced by stathmin-like proteins appears to weaken lateral contacts between tubulin subunits and could block microtubule assembly or favor disassembly. We conclude that lateral contacts between tubulin subunits in neighboring protofilaments have a decisive role for microtubule stability, rigidity, and architecture.
IT **152044-54-7**, Epothilone B
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effect of stabilizing agents on microtubule architecture)
RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

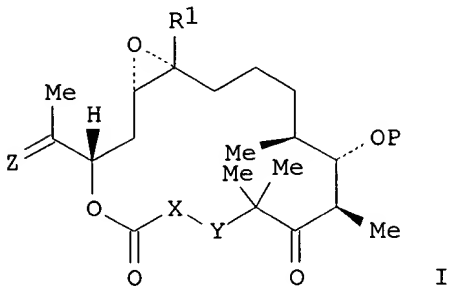


RE.CNT 6
RE
(1) Aaron, B; ANGEWANDTE CHEMIE INTERNATIONAL EDITION 1998, V37(19), P26755
(2) Dieter, S; CHEMISTRY - A EUROPEAN JOURNAL 1996, V2(11), P1477
(4) Mulzer, J; TETRAHEDRON LETTERS 1998, V39(47), P8633 CAPLUS
(5) Nicolaou, K; CHEMISTRY - A EUROPEAN JOURNAL 1997, V3(12), P1971 CAPLUS
(6) Nicolaou, K; JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 1997, V119(34), P7974 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 89 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1999:736709 CAPLUS
DN 131:336880
TI Preparation of epothilone derivatives and their use
IN Hoefle, Gerhard; Leibold, Thomas
PA Gesellschaft Fur Biotechnologische Forschung M.b.H. (Gbf), Germany
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9958534	A2	19991118	WO 1999-EP3159	19990507
	WO 9958534	A3	20000113		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19820599	A1	19991111	DE 1998-19820599	19980508
	AU 9943611	A1	19991129	AU 1999-43611	19990507

EP 1077980 A2 20010228 EP 1999-926300 19990507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI DE 1998-19820599 A 19980508
WO 1999-EP3159 W 19990507
OS CASREACT 131:336880; MARPAT 131:336880
GI



I

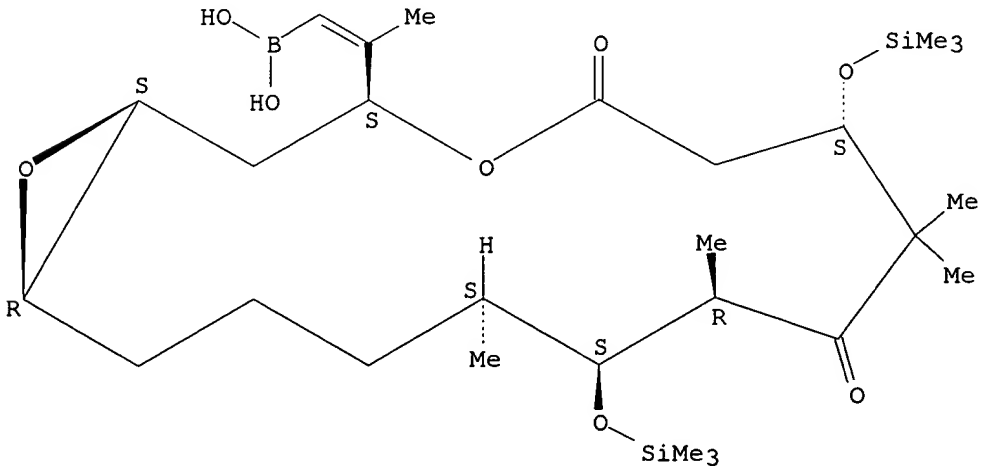
AB Epothilone derivs. I [R1 = H, C1-8 alkyl; X-Y = CH2-CH(OP)- or CH:CH; Z = CHB(OH)2, CHX1, CHR2, etc.; X1 = halo; R2 = aryl; P = H, protecting group], useful as cytostatic agents (no data) and agrochems. (no data) are prepd. Thus, I [R1 = H, X-Y = CH2-CH(OTMS), Z = O, P = TMS] was reacted with tris(ethylenedioxyboryl)methane in CH2Cl2-THF contg. BuLi at room temp. for 17 h to give 65% the boronic acid I [R1, X-Y, P same as above; Z = CHB(OH)2] (E:Z =6:4).

IT **250232-79-2P 250232-80-5P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone derivs. as plant protectants)

RN 250232-79-2 CAPLUS

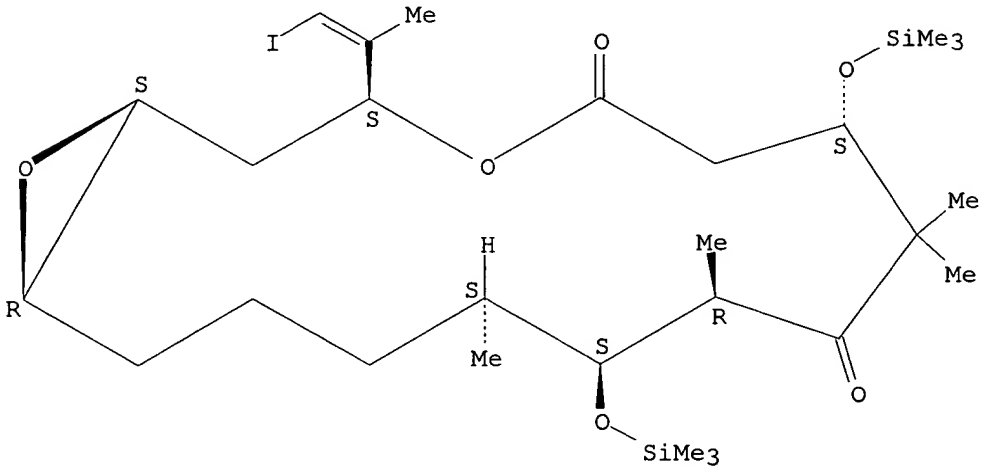
CN Boronic acid, [2-[(1S,3S,7S,10R,11S,12S,16R)-8,8,10,12-tetramethyl-5,9-dioxo-7,11-bis[(trimethylsilyl)oxy]-4,17-dioxabicyclo[14.1.0]heptadec-3-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



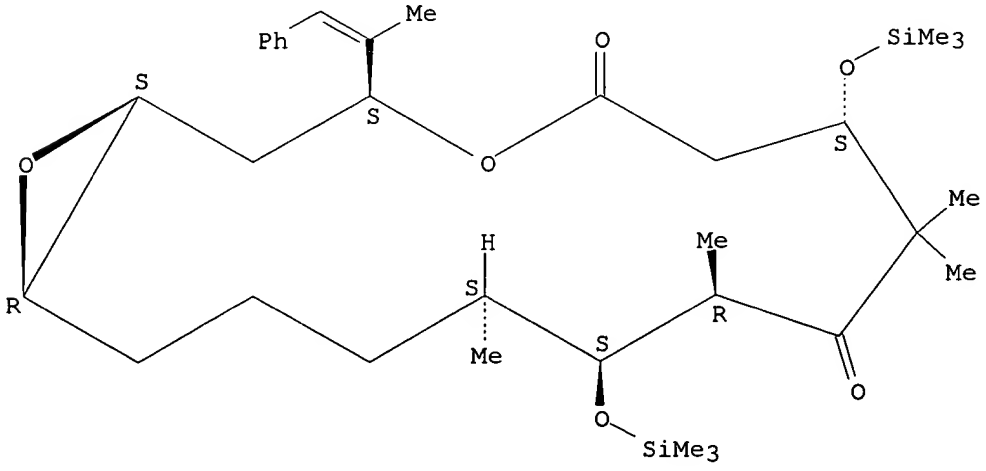
RN 250232-80-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 3-(2-iodo-1-methylethenyl)-8,8,10,12-tetramethyl-7,11-bis[(trimethylsilyl)oxy]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

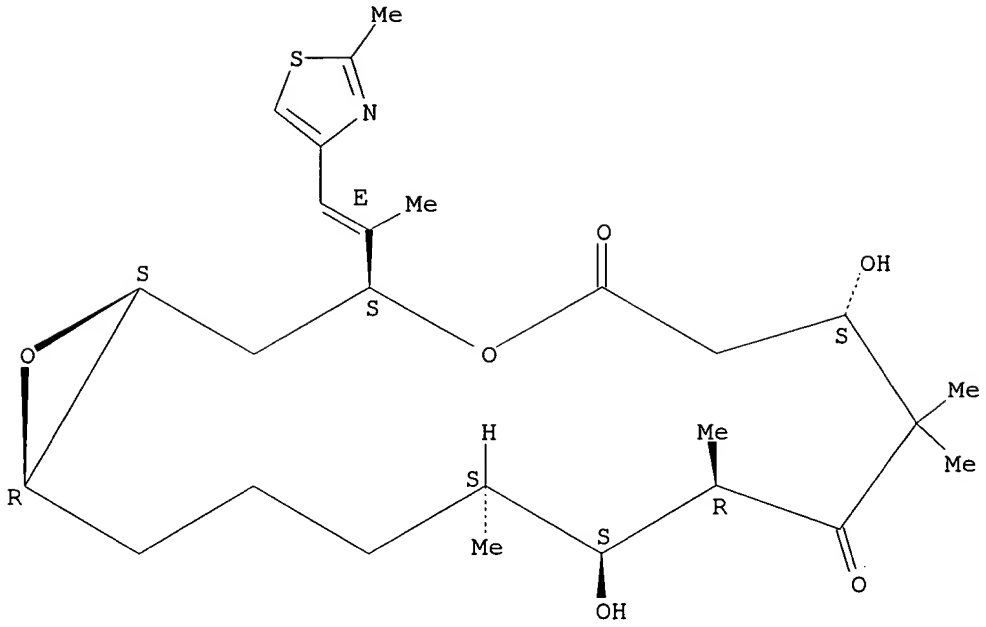


IT **250232-82-7P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone derivs. as plant protectants)
RN 250232-82-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 8,8,10,12-tetramethyl-3-(1-methyl-2-phenylethenyl)-7,11-bis[(trimethylsilyl)oxy]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

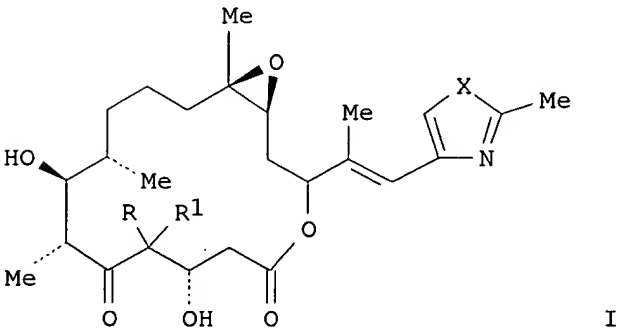
Absolute stereochemistry.
Double bond geometry unknown.



L4 ANSWER 90 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1999:733952 CAPLUS



L4 ANSWER 163 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1998:50907 CAPLUS
DN 128:180246
TI Total synthesis of oxazole- and cyclopropane-containing epothilone B analogs by the macrolactonization approach
AU Nicolaou, K. C.; Sarabia, Francisco; Finlay, M. Ray V.; Ninkovic, Sacha; King, N. Paul; Vourloumis, Dionisios; He, Yun
CS Department of Chemistry and The Skaggs Institute for Chemical Biology The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chem.--Eur. J. (1997), 3(12), 1971-1986
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
GI



I

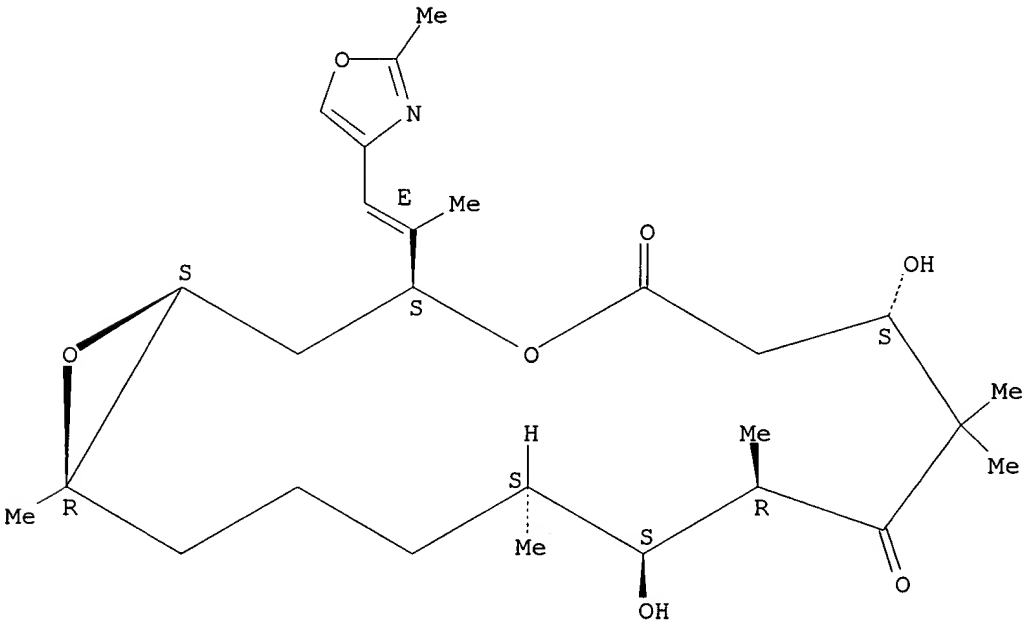
AB In order to probe structure-activity relationships in the epothilone area, two series of epothilone B analogs were designed and synthesized. The first series contg. an oxazole moiety in place of a thiazole on the side

chain was constructed via utilization of key intermediates whereas the second series contg. an ethano group instead of the gem-di-Me group at position 4 was synthesized. A Yamaguchi-type macrolactonization reaction was used to construct the macrocycle from a secoacid, which was assembled, in both cases, via a) an aldol reaction, b) an Enders alkylation, and c) a Wittig-type reaction. This convergent strategy provided access to oxazole and 4,4-ethano analogs, e.g., I (R = R1 = Me, X = O, S; RR1 = CH2CH2, X = O, S).

IT **198571-00-5P 198571-01-6P 198571-06-1P 203252-75-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of oxazole- and cyclopropane-contg. epothilone B analogs via macrolactonization)

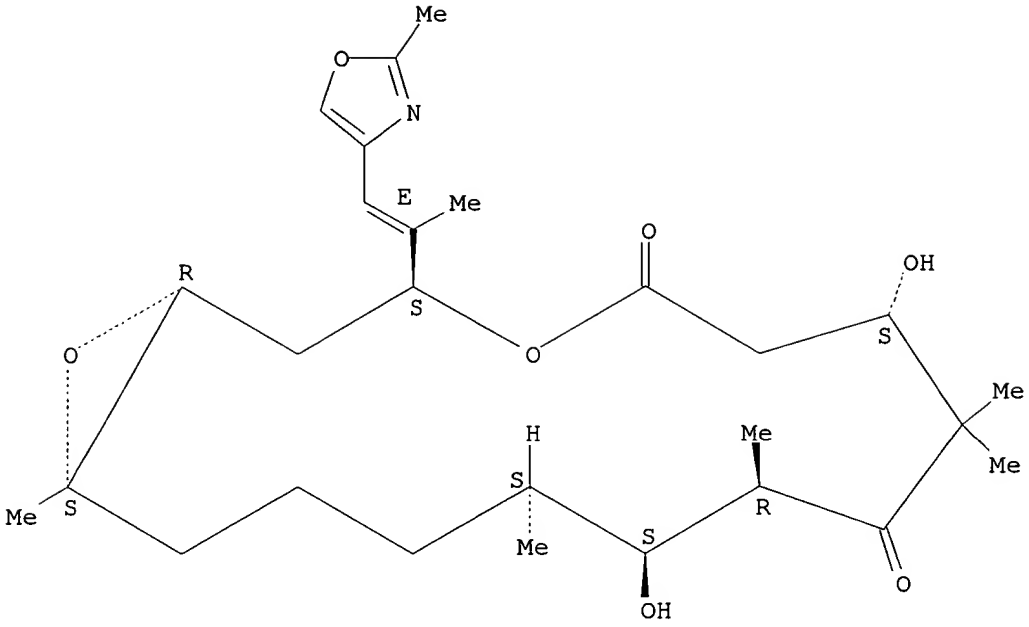
RN 198571-00-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



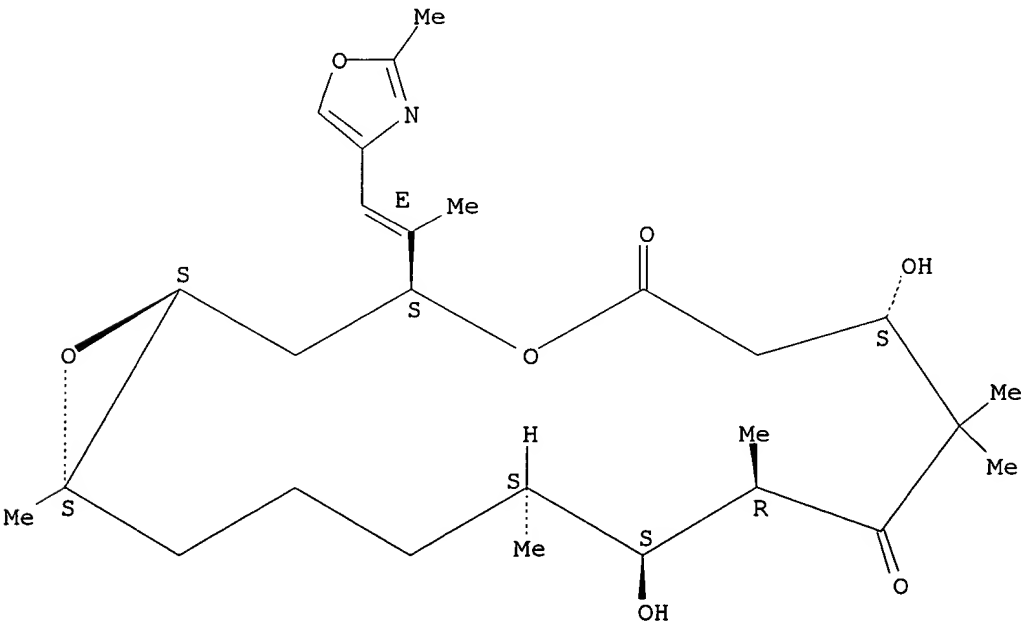
RN 198571-01-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



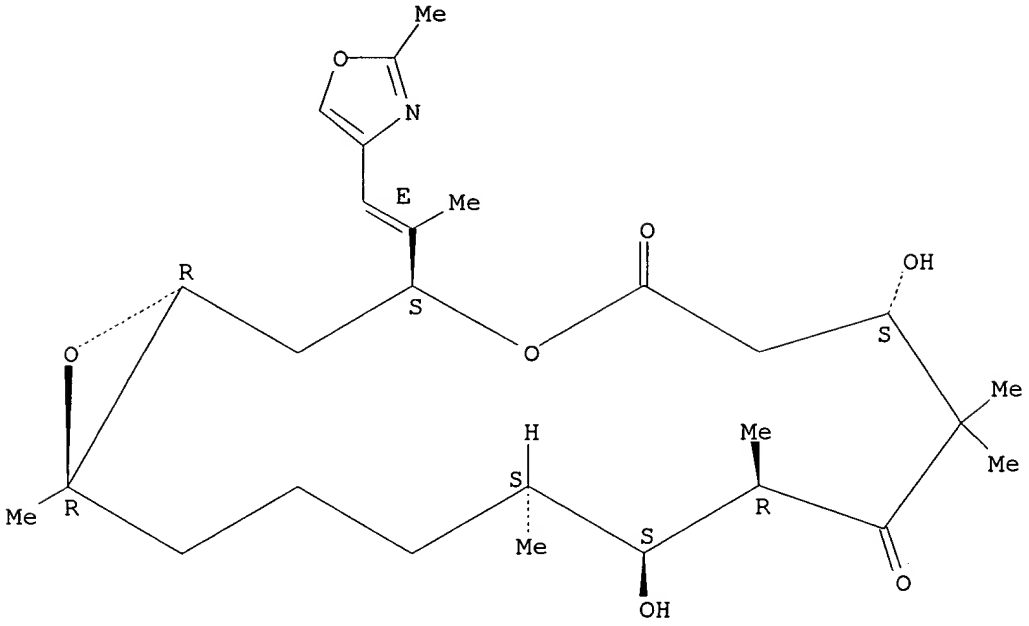
RN 198571-06-1 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

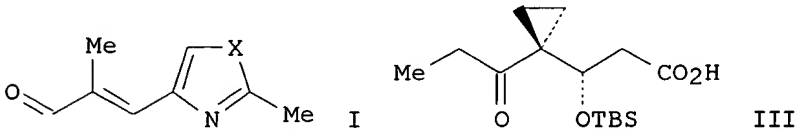


RN 203252-75-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 164 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1998:50906 CAPLUS
DN 128:140541
TI Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach
AU Nicolaou, K. C.; Vallberg, Hans; King, N. Paul; Roschangar, Frank; He, Yun; Vourloumis, Dionisios; Nicolaou, Christopher G.
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Chem.--Eur. J. (1997), 3(12), 1957-1970
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
GI



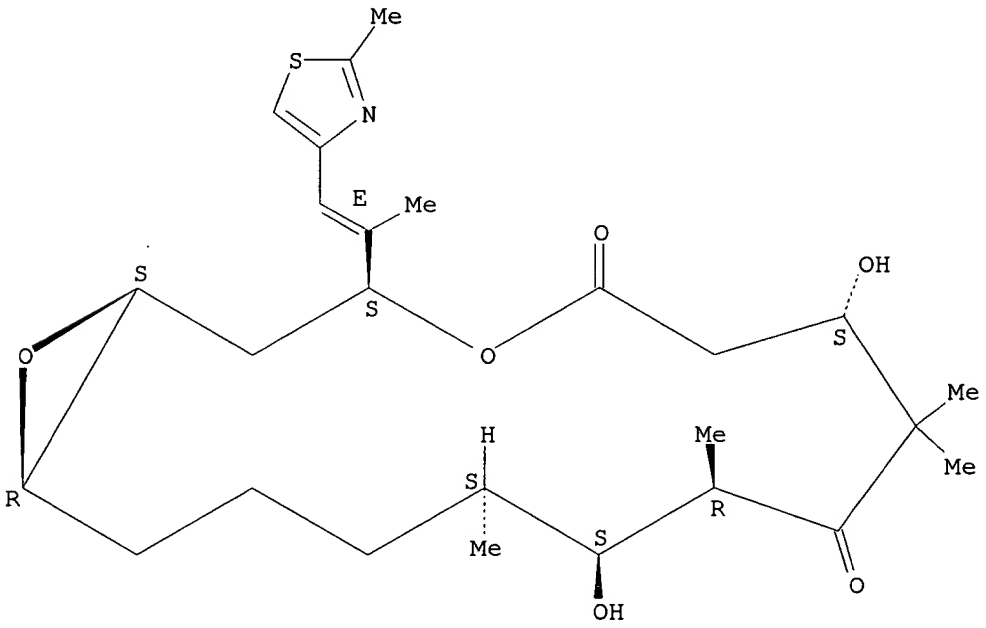
AB For structure-activity relationship studies, two series of epothilone A analogs have been designed and synthesized, one contg. an oxazole moiety instead of the thiazole heterocycle and the other contg. a spirocyclopropane moiety in place of the gem-di-Me group at position C-4 (4,4-ethano-epothilones). The olefin metathesis strategy in soln. was utilized for the chem. synthesis of these compds. starting with key building blocks (I) (X = O), (S)-H2C=CH(CH2)3CH(Me)CHO (II),

(S)-MeCH2COCMe2CH(OSiMe2CMe3)CH2CO2H for the oxazole series and building blocks I (X = S), II, and (III) for the 4,4-ethano series. The convergent strategy towards the designed epothilone A series involved: a- an aldol condensation reaction, b- an esterification reaction, c- an olefin metathesis reaction catalyzed by [RuCl2(=CHPh)-(PCy3)2], and d- epoxidn. of the macrocycle double bond.

IT **152044-53-6DP**, Epothilone A, analogs **198570-99-9P** **198571-02-7P** **198571-05-0P** **198571-07-2P** **202333-48-0P** **202333-49-1P** **202333-50-4P** **202333-51-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of oxazole- and cyclopropane-contg. epothilone A analogs by the olefin metathesis approach)

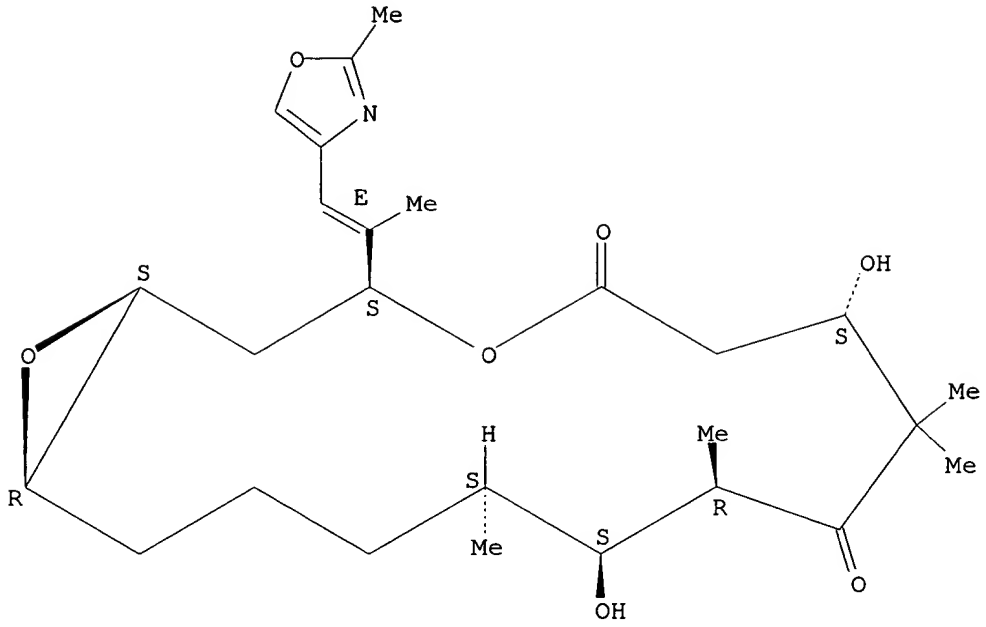
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



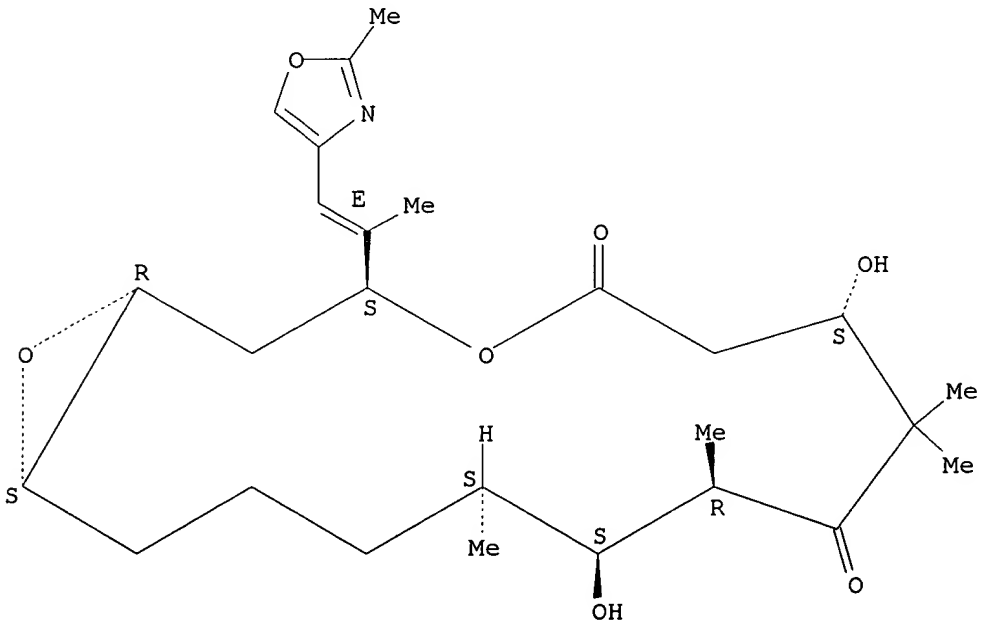
RN 198570-99-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



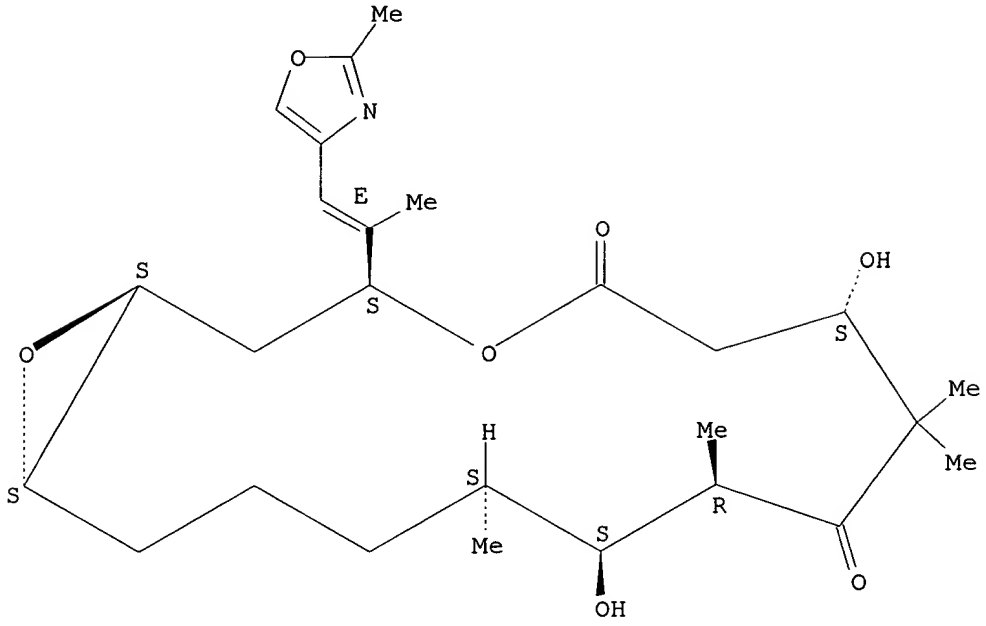
RN 198571-02-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



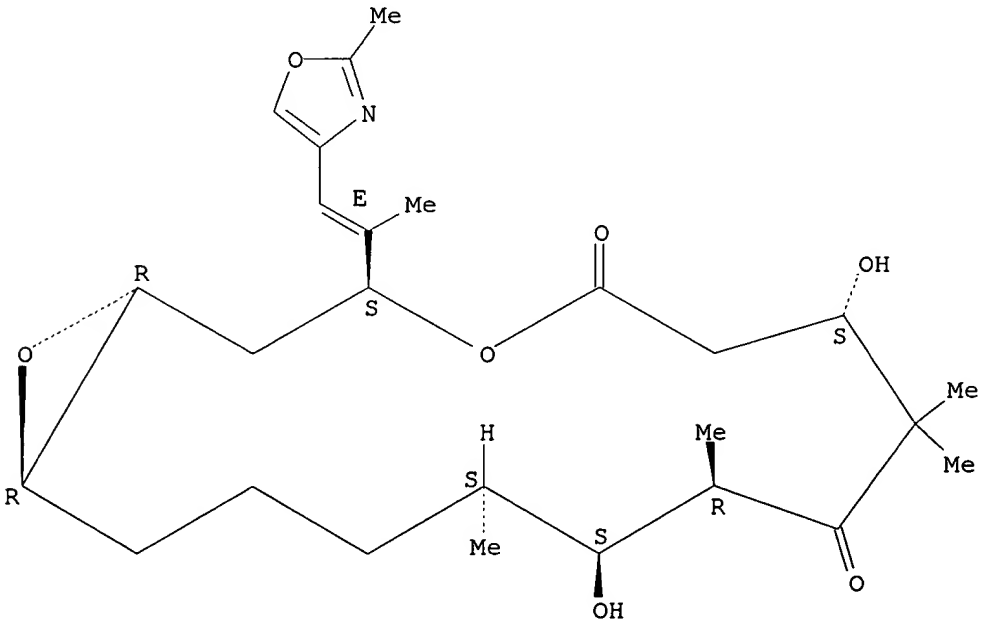
RN 198571-05-0 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-07-2 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

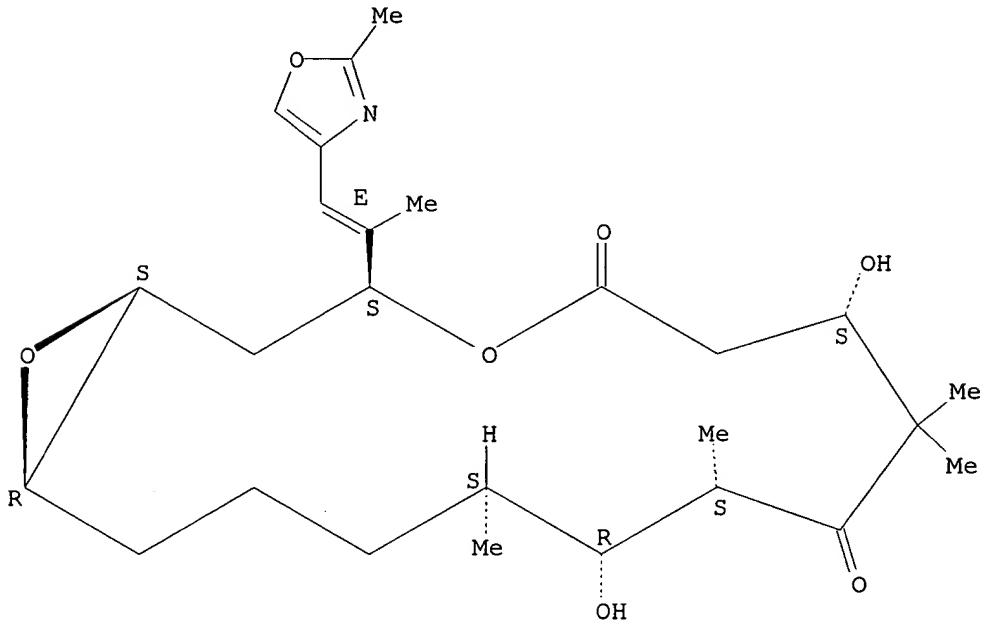
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-48-0 CAPLUS

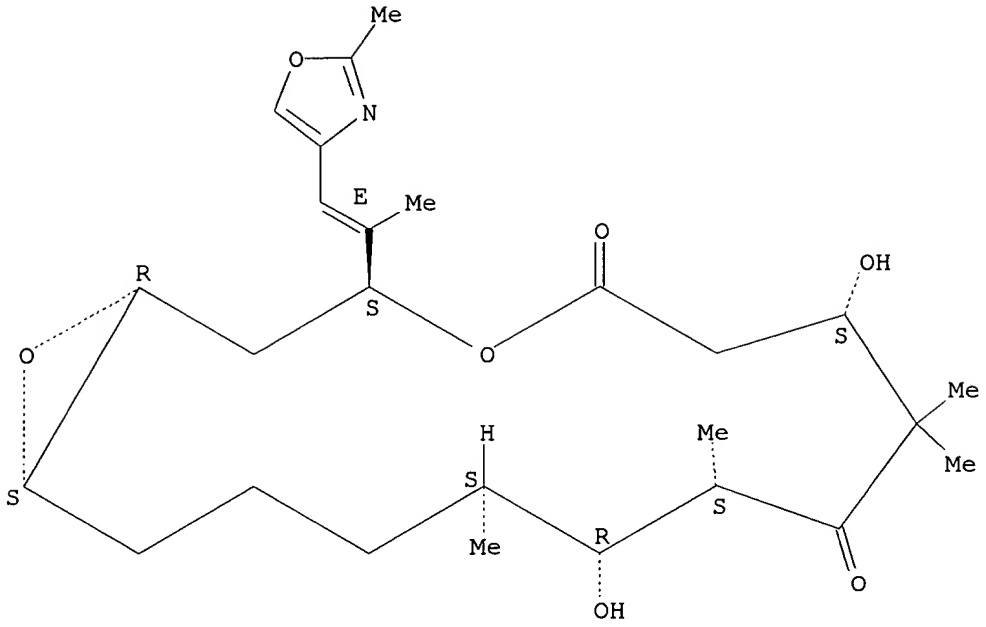
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [1S-[1R*,3R*(E),7R*,10R*,11S*,12R*,16S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



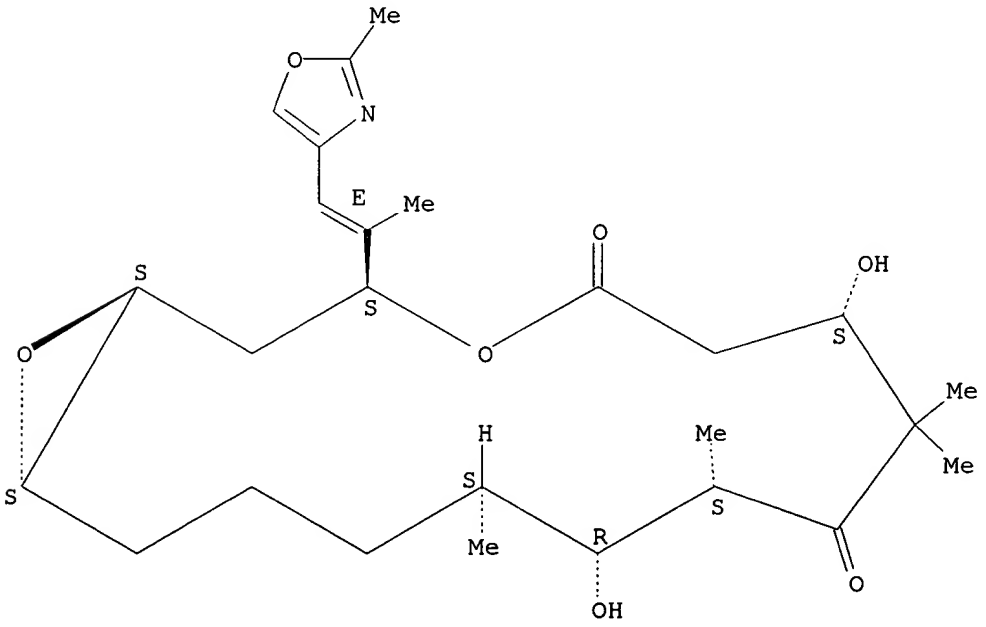
RN 202333-49-1 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [1R-[1R*,3S*(E),7S*,10S*,11R*,12S*,16S*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



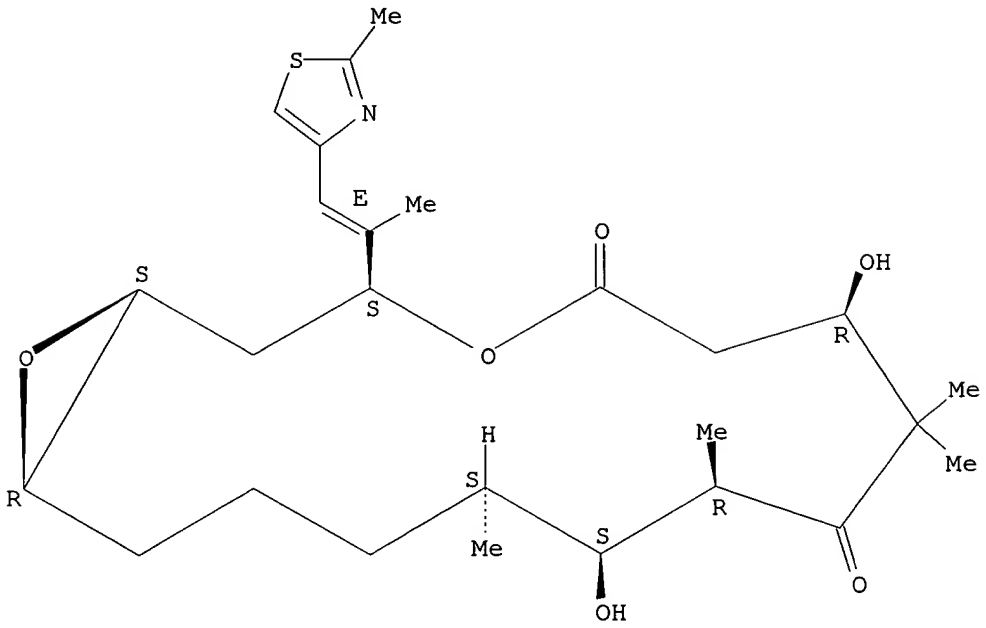
RN 202333-50-4 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [1S-[1R*,3R*(E),7R*,10R*,11S*,12R*,16R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-51-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [1R-[1R*,3S*(E),7S*,10S*,11R*,12S*,16R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 176 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:623009 CAPLUS
DN 127:268036
TI Water soluble paclitaxel prodrugs
IN Li, Chun; Wallace, Sidney; Yu, Dong-Fang
PA Wallace Technologies, Inc., USA; Li, Chun; Wallace, Sidney; Yu, Dong-Fang
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9733552	A1	19970918	WO 1997-US3687	19970311
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2250295	AA	19970918	CA 1997-2250295	19970311
	AU 9725806	A1	19971001	AU 1997-25806	19970311
	CN 1217662	A	19990526	CN 1997-194360	19970311
	EP 932399	A1	19990804	EP 1997-917512	19970311
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 5977163	A	19991102	US 1997-815104	19970311
	BR 9710646	A	20000111	BR 1997-10646	19970311
	JP 2000507930	T2	20000627	JP 1997-532734	19970311
	NO 9804210	A	19981111	NO 1998-4210	19980911

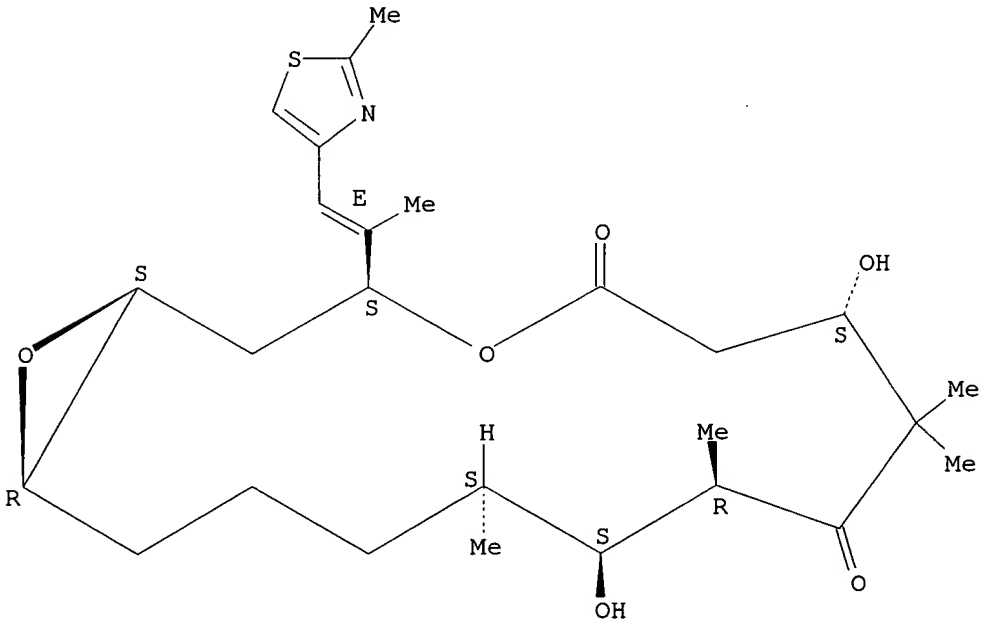
US 6262107 B1 20010717 US 1999-346263 19990701
PRAI US 1996-13184 P 19960312
US 1997-815104 A1 19970311
WO 1997-US3687 W 19970311

AB Disclosed are water sol. compns. of paclitaxel and docetaxel formed by conjugating the paclitaxel or docetaxel to a water sol. chelator, polyethylene glycol or polymer such as poly(L-glutamic acid) or poly(L-aspartic acid). Also disclosed are methods of using the compns. for treatment of tumors, autoimmune disorders such as rheumatoid arthritis and for prediction of paclitaxel uptake by tumors and radiolabeled DTPA-paclitaxel tumor imaging. Other embodiments include the coating of implantable stents for prevention of restenosis. A conjugate of DTPA and paclitaxel was prepd. and tested for antitumor activity.

IT **152044-53-6**, Epothilone A **152044-54-7**, Epothilone B
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(water sol. paclitaxel prodrugs)

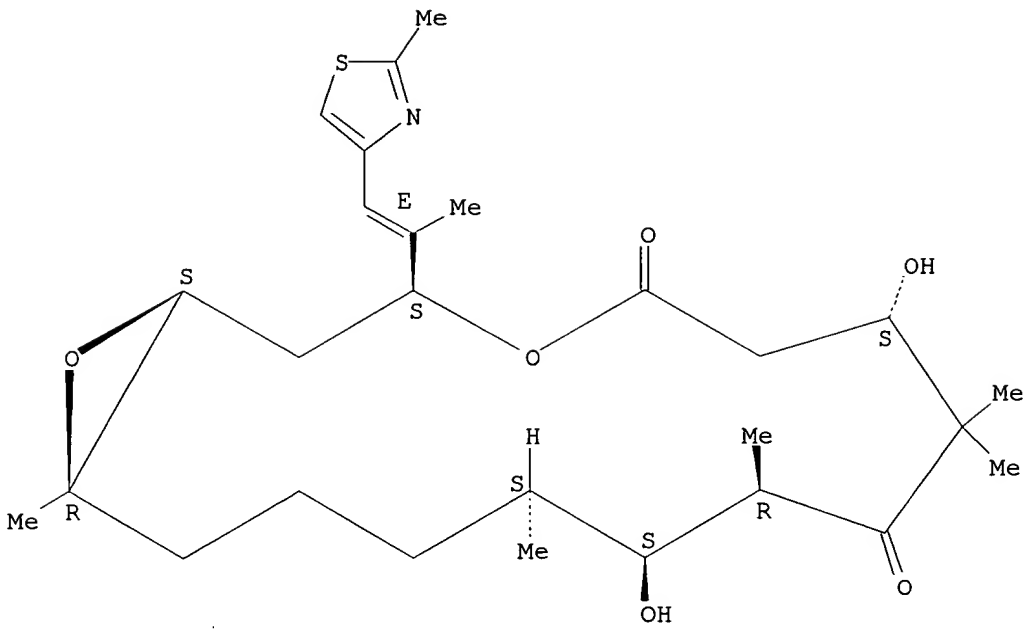
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

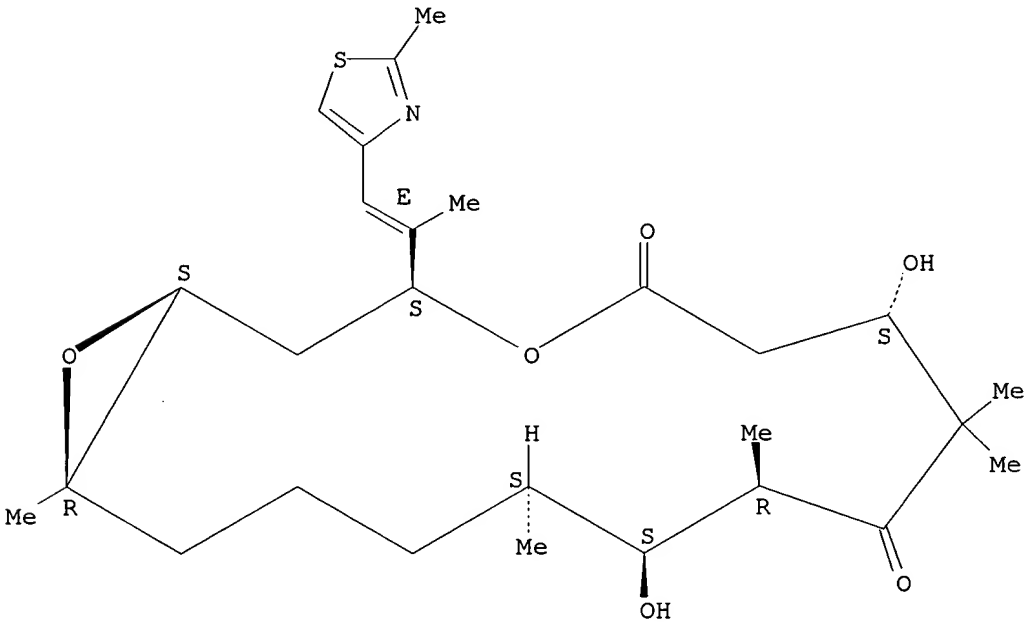
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 177 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:560269 CAPLUS
DN 127:242883
TI Epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity
AU Muhlradt, Peter F.; Sasse, Florenz
CS Gesellschaft fur Biotechnologische Forschung mbH, Arbeitsgruppe Immunbiologie, Braunschweig, D-38124, Germany
SO Cancer Res. (1997), 57(16), 3344-3346
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Epothilones are a new class of potential antitumor compds. that were isolated from the myxobacterium Sorangium cellulosum. Epothilones have effects on the cytoskeleton similar to those of the antineoplastic drug Taxol. Both compds. inhibit cell proliferation by stabilizing microtubuli, and they compete for the same binding site. In addn., Taxol displays endotoxin-like properties in that it activates macrophages to synthesize proinflammatory cytokines and nitric oxide. We measured nitric oxide release by IFN-.gamma.-treated murine macrophages as an indicator of macrophage activation by epothilone B. Although epothilone B showed the expected effects on the microtubuli, there was no indication of macrophage stimulatory activity by epothilone B, nor did epothilone B inhibit lipopolysaccharide-mediated nitric oxide release. We conclude that, unlike Taxol, epothilone-mediated microtubuli stabilization does not trigger endotoxin-signaling pathways. Moreover, because the endotoxin-like activity of Taxol may be the cause of some nonhematol. clin. side effects, it is to be expected that such effects may not occur with epothilones.
IT **152044-54-7**, Epothilone B
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epothilone B stabilizes microtubili of macrophages like taxol without showing taxol-like endotoxin activity in relation to antitumor

activity)
RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 178 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:528753 CAPLUS
DN 127:135660
TI Total Syntheses of Epothilones A and B via a Macrolactonization-Based Strategy
AU Nicolaou, K. C.; Ninkovic, S.; Sarabia, F.; Vourloumis, D.; He, Y.; Vallberg, H.; Finlay, M. R. V.; Yang, Z.
CS Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SO J. Am. Chem. Soc. (1997), 119(34), 7974-7991
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:135660
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total syntheses of epothilones A (I) (R = H) and B I (R = Me) and several analogs are described. The reported strategy relies on a macrolactonization approach and features selective epoxidn. of the macrocycle double bond in precursors II (R = H, Me) as well as high convergency and flexibility. Building blocks (S)-

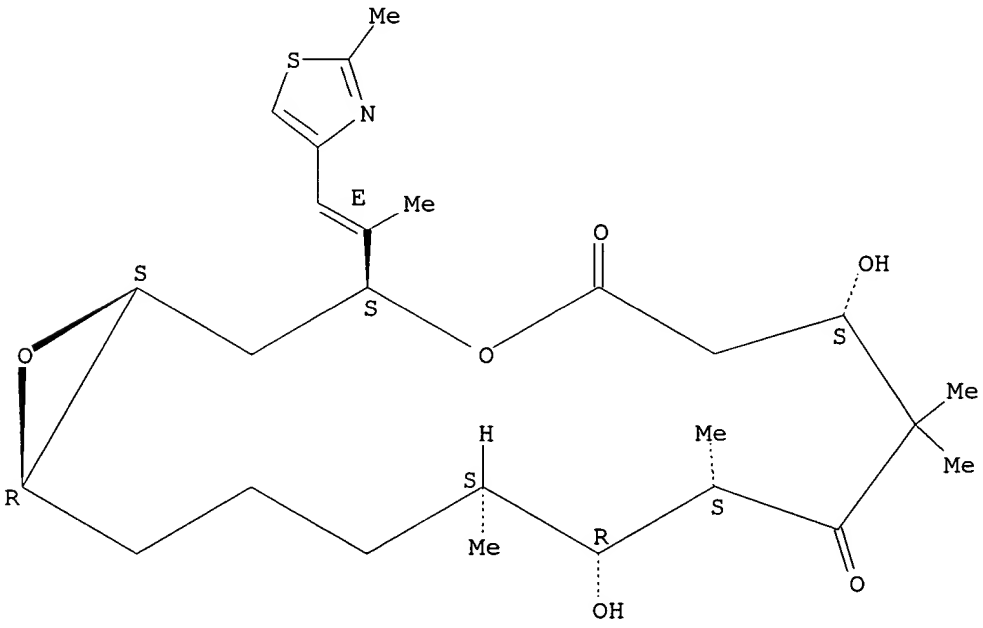
MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H, (S)-Me3CMe2SiOCH2CH(Me)CH2CH2CH2COR (R = H, Me), (III) [R2 = CH2CH2P+(Ph)3I-; CH2CHO] were constructed by asym. processes and coupled via Wittig, aldol, and macrolactonization reactions to afford the basic skeleton of epothilones and that of several of their analogs by a relatively short route. The utilization of intermediate III [R2 = (E)-CH2CH=C(Me)CH2CH2CH2I], obtained via a stereoselective Wittig reaction and its Enders coupling to SAMP hydrazone, in combination with a stereoselective aldol reaction with the modified substrate (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CH2OSiMe2CMe3 improved the stereoselectivity and efficiency of the total synthesis of these new and highly potent microtubule binding antitumor agents.

IT **193146-36-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total syntheses of epothilones A and B via a macrolactonization-based strategy)

RN 193146-36-0 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10S,11R,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

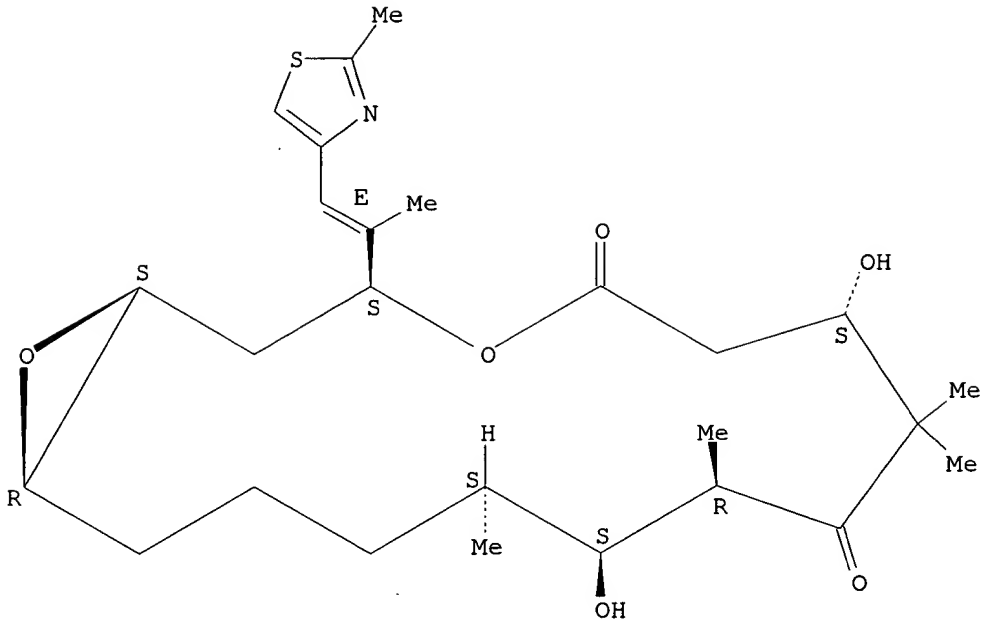


IT **152044-53-6P**, Epothilone A **152044-54-7P**, Epothilone B **190370-10-6P 190370-11-7P 190370-13-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total syntheses of epothilones A and B via a macrolactonization-based strategy)

RN 152044-53-6 CAPLUS

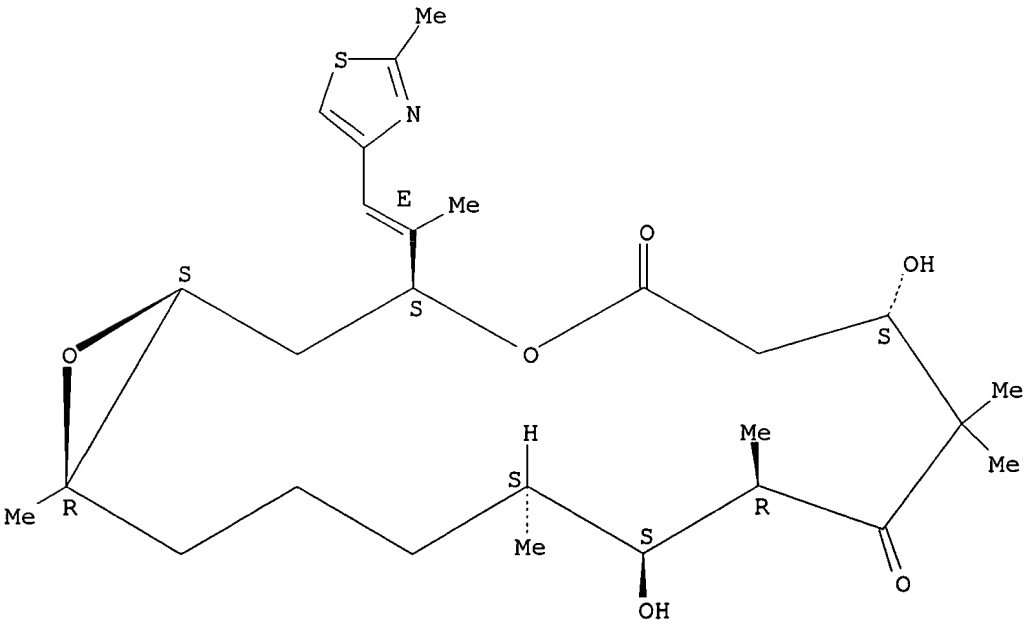
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



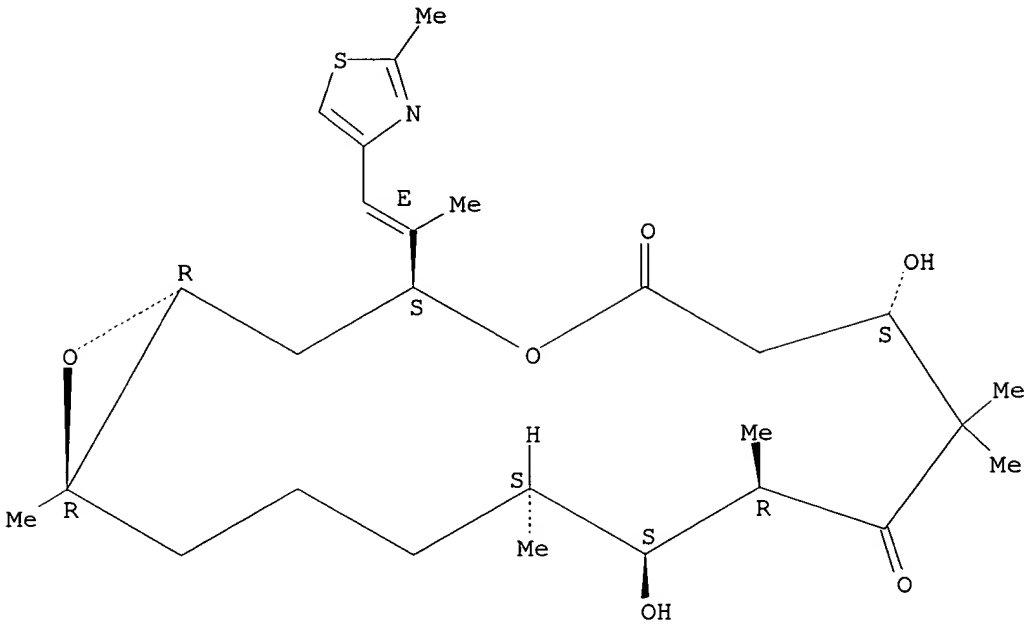
RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



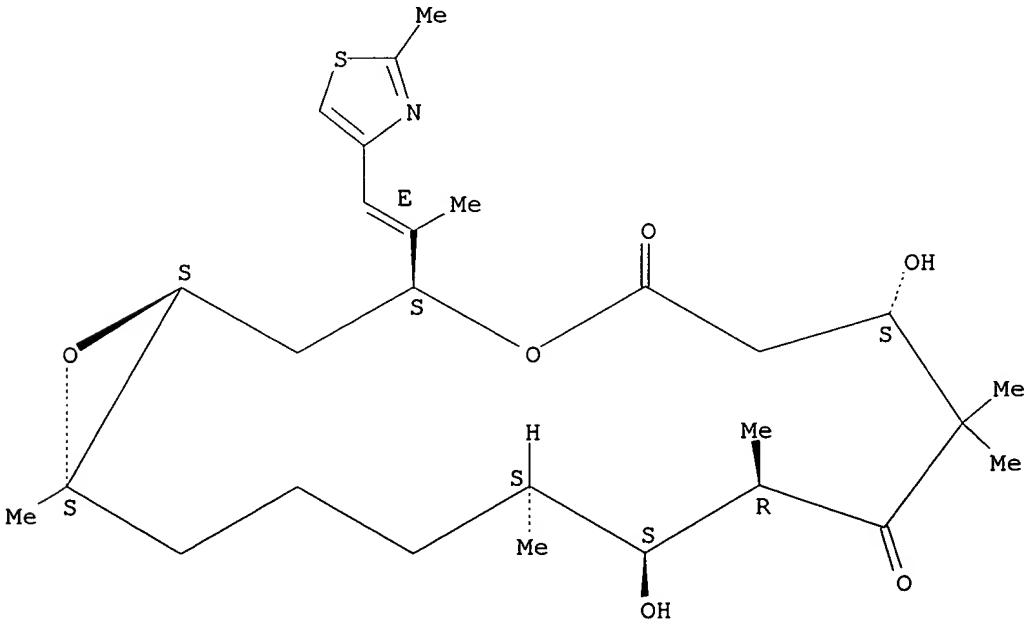
RN 190370-10-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190370-11-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

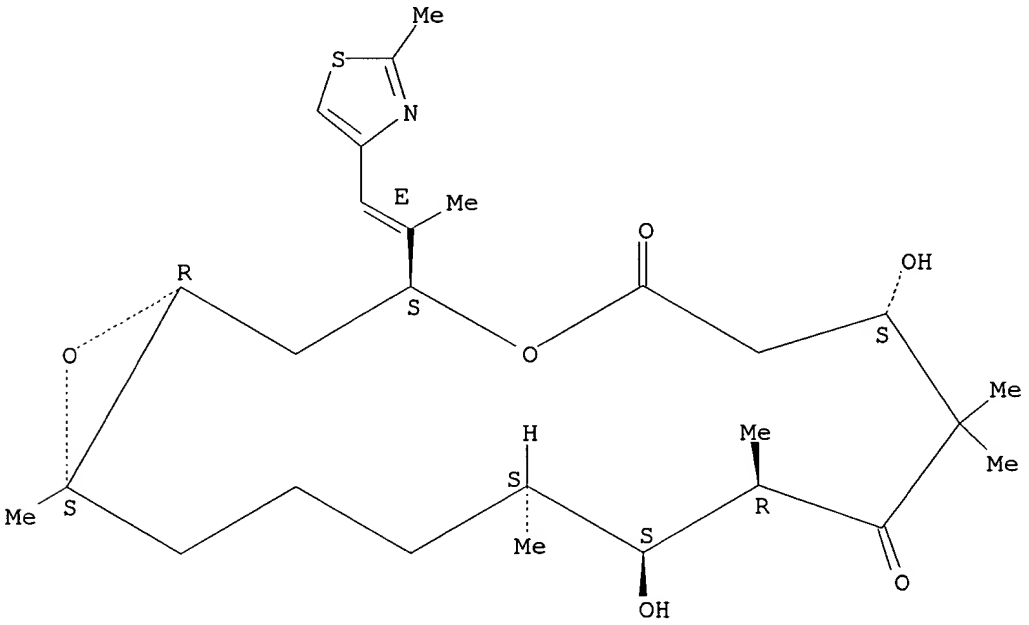
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190370-13-9 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

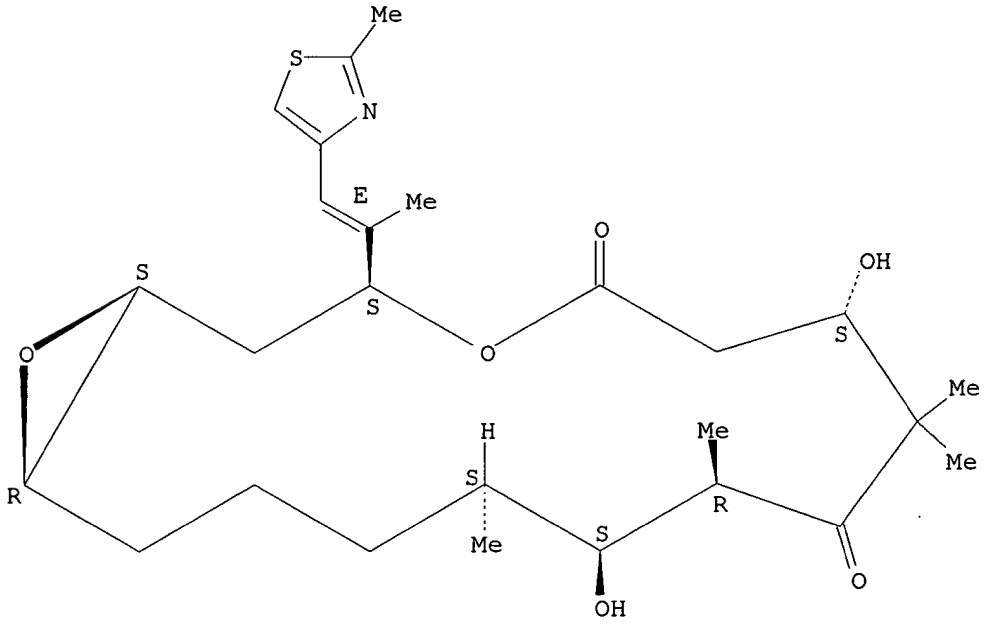


L4 ANSWER 179 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:528752 CAPLUS
DN 127:149021
TI The Olefin Metathesis Approach to Epothilone A and Its Analogs
AU Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; S.Ninkovic,; Yang, Z.; Trujillo, J. I.
CS Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SO J. Am. Chem. Soc. (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 127:149021
GI For diagram(s), see printed CA Issue.
AB The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II, (S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compd. III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.
IT **152044-53-6P**, Epothilone A **190369-91-6P**
193071-68-0P 193071-69-1P 193071-71-5P

193071-72-6P 193071-75-9P 193071-82-8P
193071-87-3P 193071-88-4P 193071-89-5P
193071-90-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)

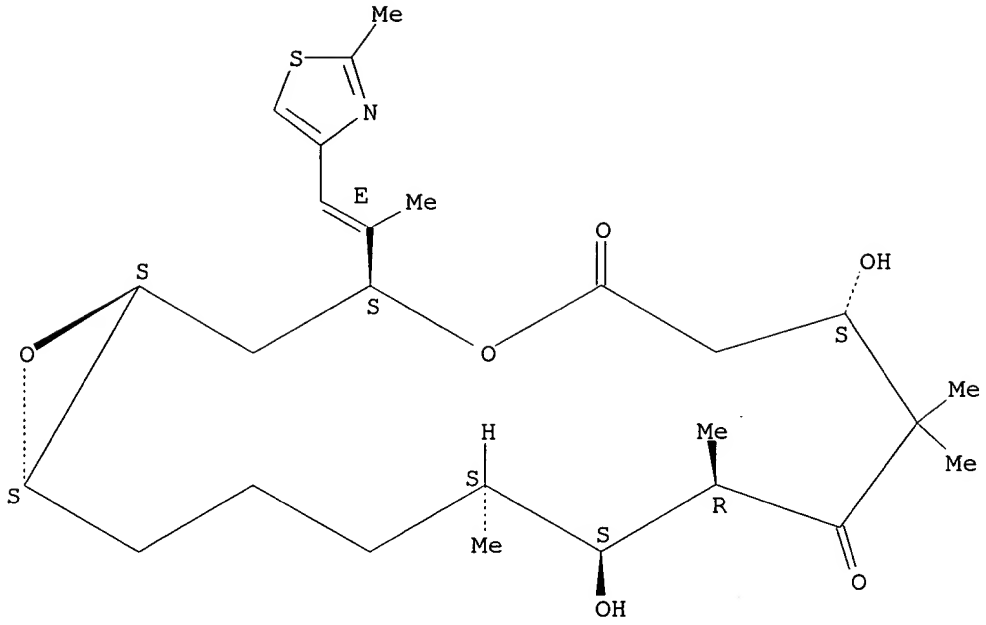
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



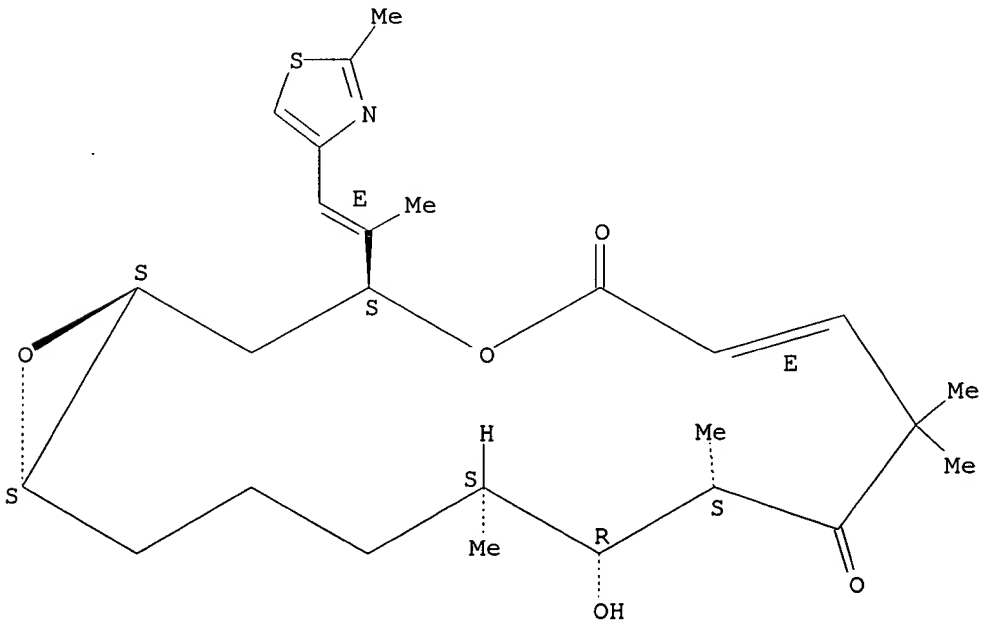
RN 190369-91-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



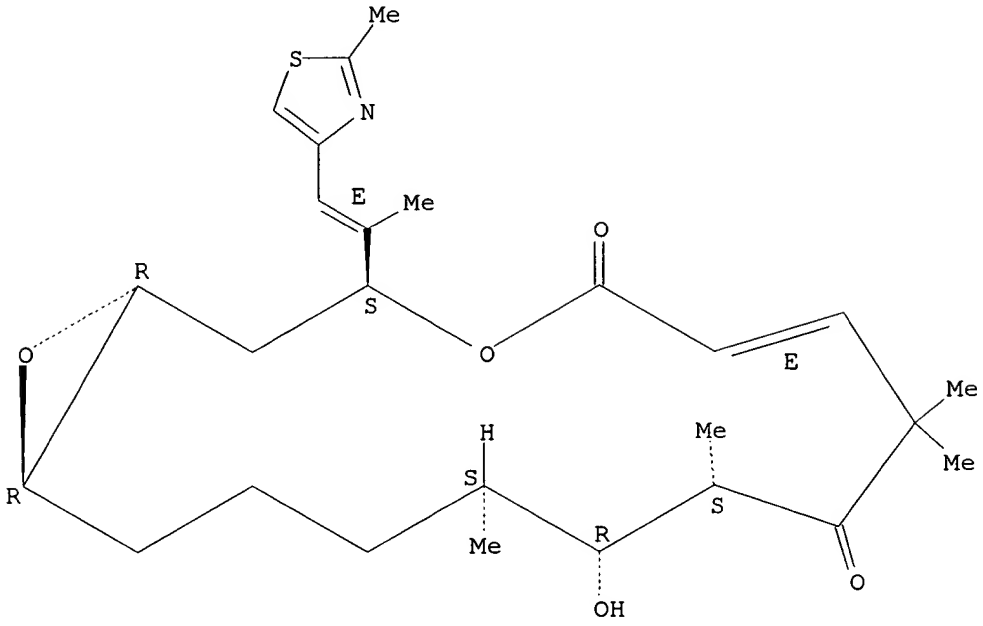
RN 193071-68-0 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10S,11R,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



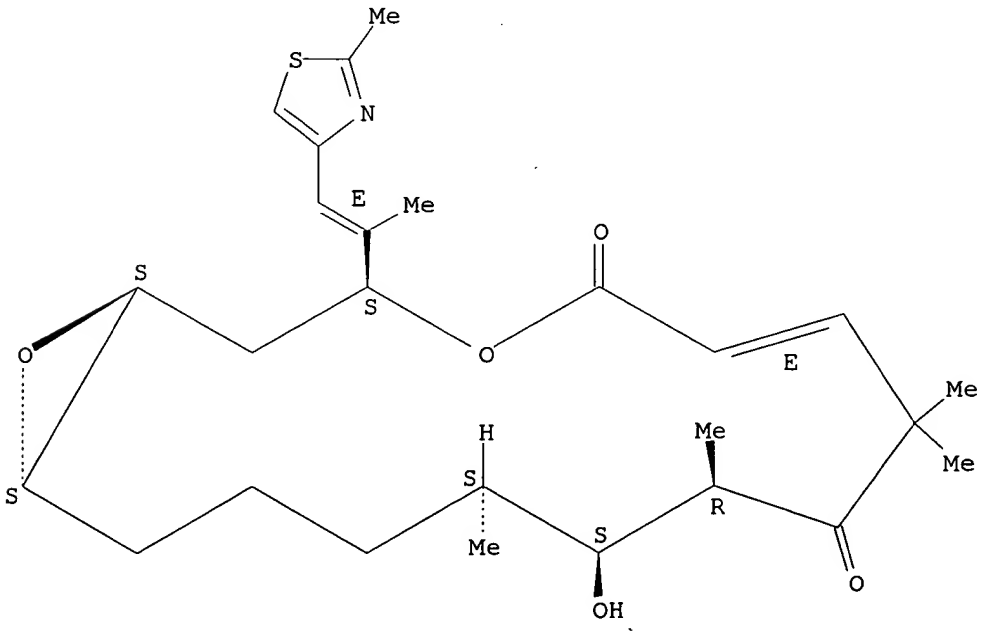
RN 193071-69-1 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10S,11R,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 193071-71-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,6E,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

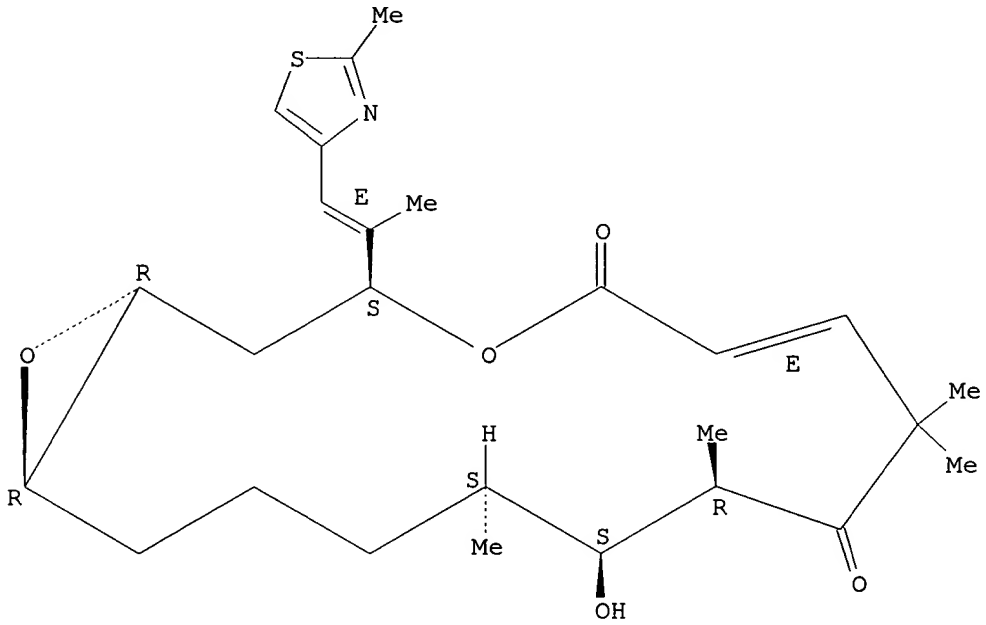
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 193071-72-6 CAPLUS

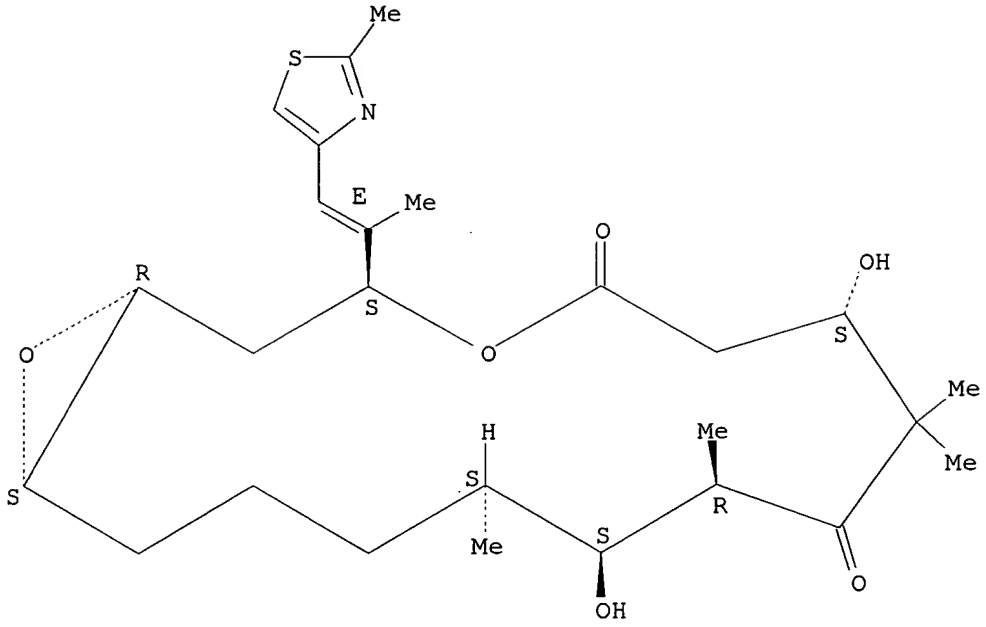
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,6E,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



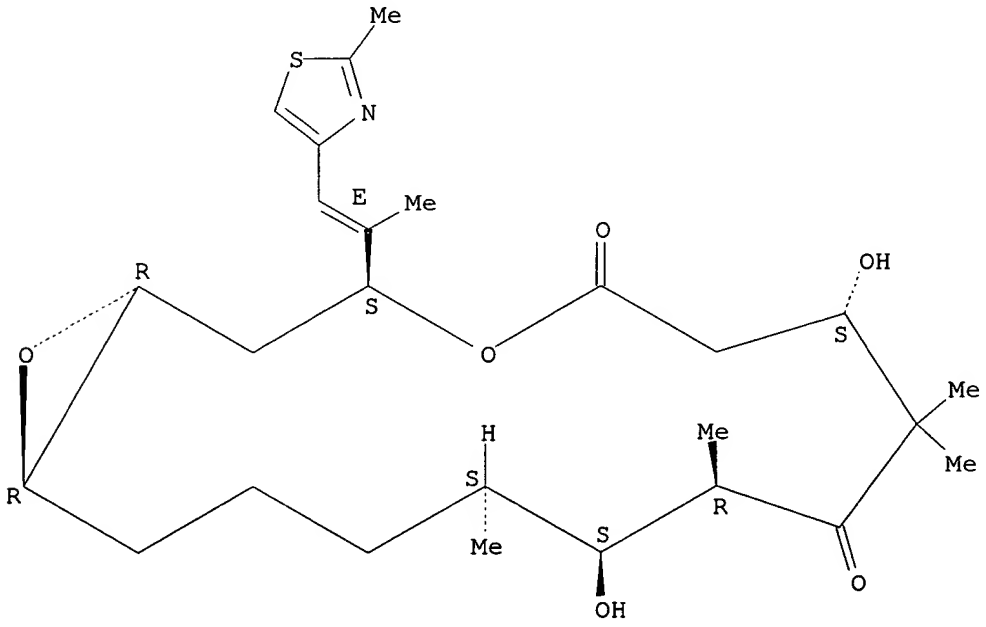
RN 193071-75-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



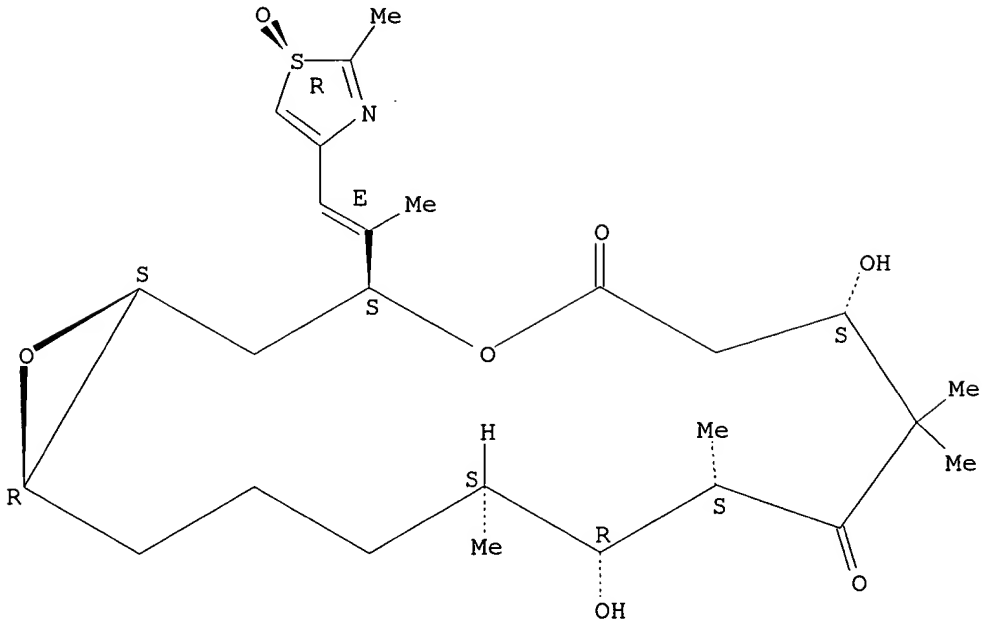
RN 193071-82-8 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



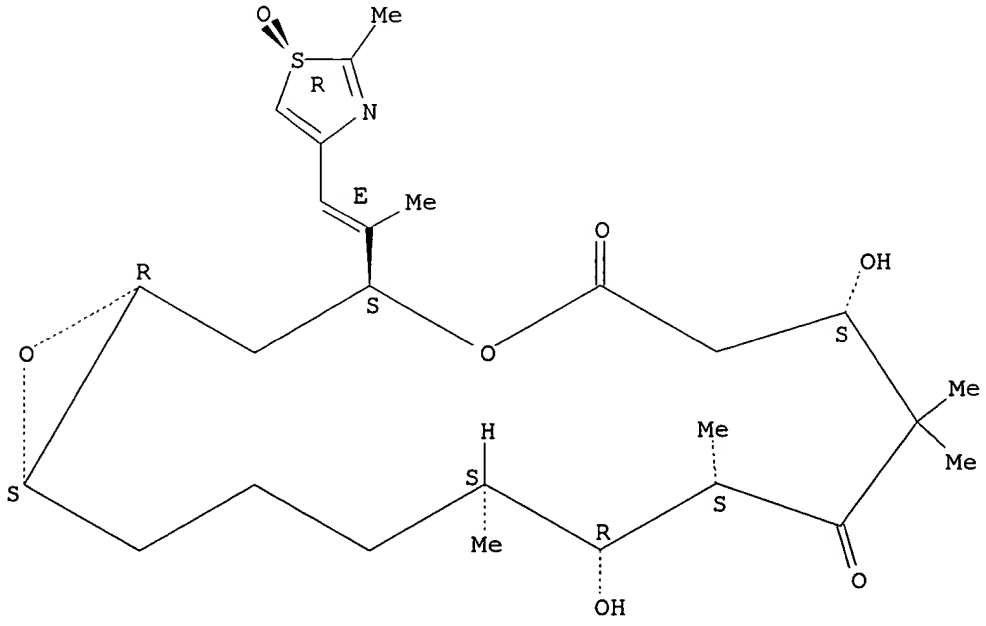
RN 193071-87-3 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (1S,3S,7S,10S,11R,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 193071-88-4 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (1R,3S,7S,10S,11R,12S,16S)- (9CI) (CA INDEX NAME)

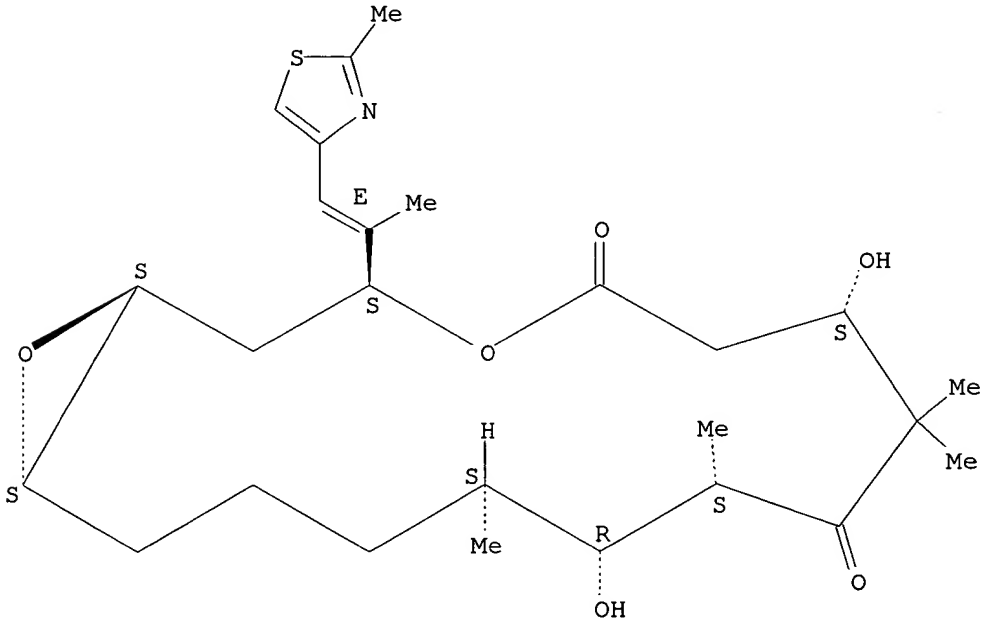
Absolute stereochemistry.
Double bond geometry as shown.



RN 193071-89-5 CAPLUS

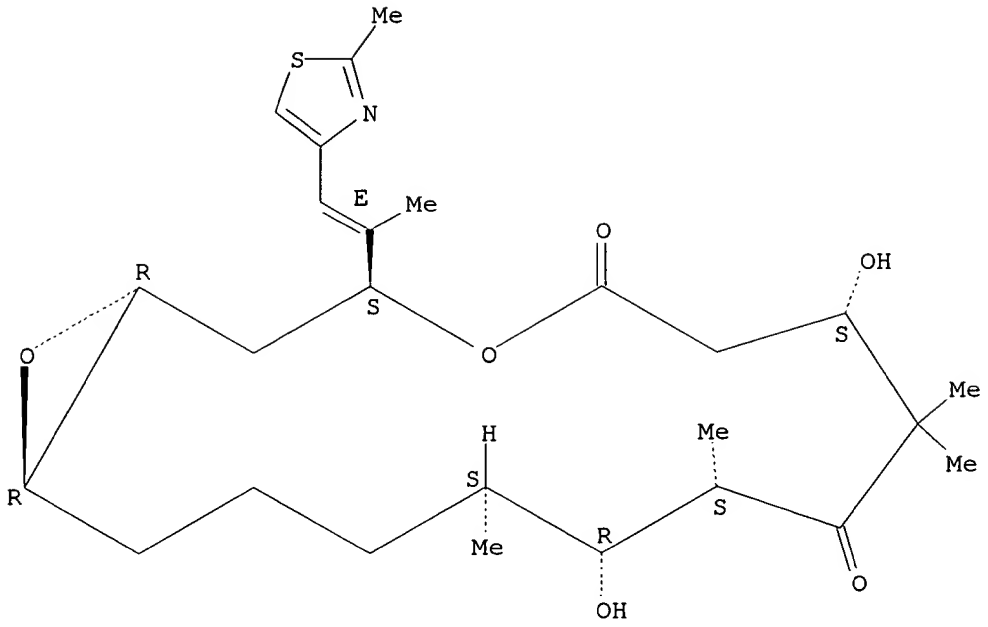
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10S,11R,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



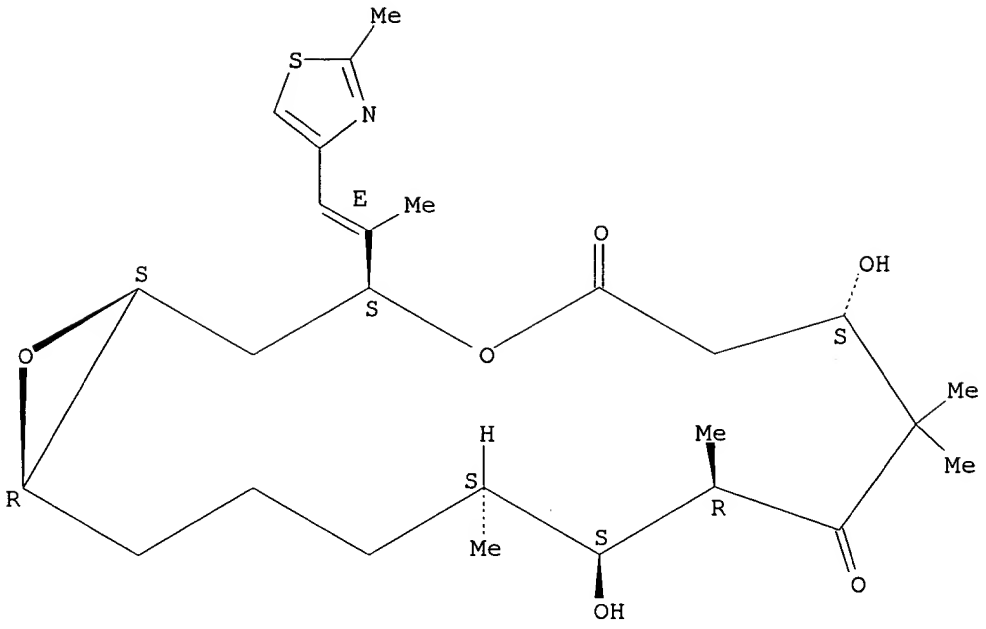
RN 193071-90-8 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10S,11R,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 180 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:522243 CAPLUS
DN 127:234203
TI Towards a synthesis of epothilone A. Rapid assembly of the C(1)-C(6) and C(7)-C(12) fragments
AU De Brabander, Jef; Rosset, Stephane; Bernardinelli, Gerald
CS Departement Chimie Organique, Universite Geneve, Geneva, CH-1211, Switz.
SO Synlett (1997), (7), 824-826
CODEN: SYNLES; ISSN: 0936-5214
PB Thieme
DT Journal
LA English
OS CASREACT 127:234203
AB A short 4-step synthesis of the C(1)-C(6) and C(7)-C(12) fragments of epothilone A, starting from a bornane-10,2-sultam, was achieved in 77 and 56% overall yield resp.
IT **152044-53-6P**, Epothilone A
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of epothilone A fragments)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

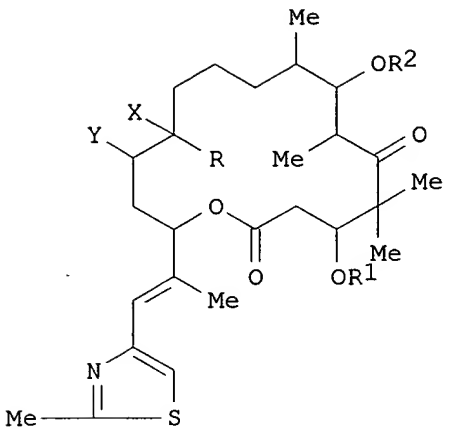
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 181 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:456769 CAPLUS
DN 127:50474
TI Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
IN Hoefle, Gerhard; Kiffe, Michael
PA Gesellschaft fuer Biotechnologische Forschung Mbh (Gbf), Germany
SO Ger. Offen., 9 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19542986	A1	19970522	DE 1995-19542986	19951117
	WO 9719086	A1	19970529	WO 1996-EP5080	19961118
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 873341	A1	19981028	EP 1996-939097	19961118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 903348	A1	19990324	EP 1998-121523	19961118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000500757	T2	20000125	JP 1997-519381	19961118
PRAI	DE 1995-19542986		19951117		
	DE 1996-19639456		19960925		
	EP 1996-939097		19961118		
	WO 1996-EP5080		19961118		

OS MARPAT 127:50474
GI



I

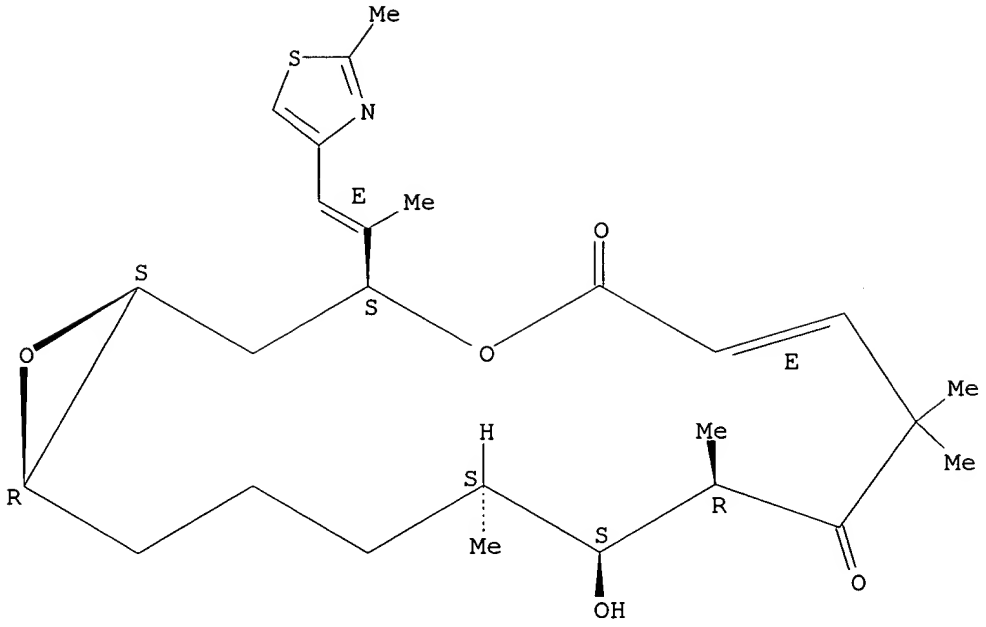
AB The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = halo, OH, acyloxy, alkoxy, benzoyloxy] , useful as agrochems. and pharmaceuticals (no data), are prepd. Thus, epothilone A in acetone contg. trifluoroacetic acid was heated overnight at 50.degree. and the reaction mixt. was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT **191105-88-1P 191105-89-2P 191105-90-5P**
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone derivs. as agrochems. and pharmaceuticals)

RN 191105-88-1 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

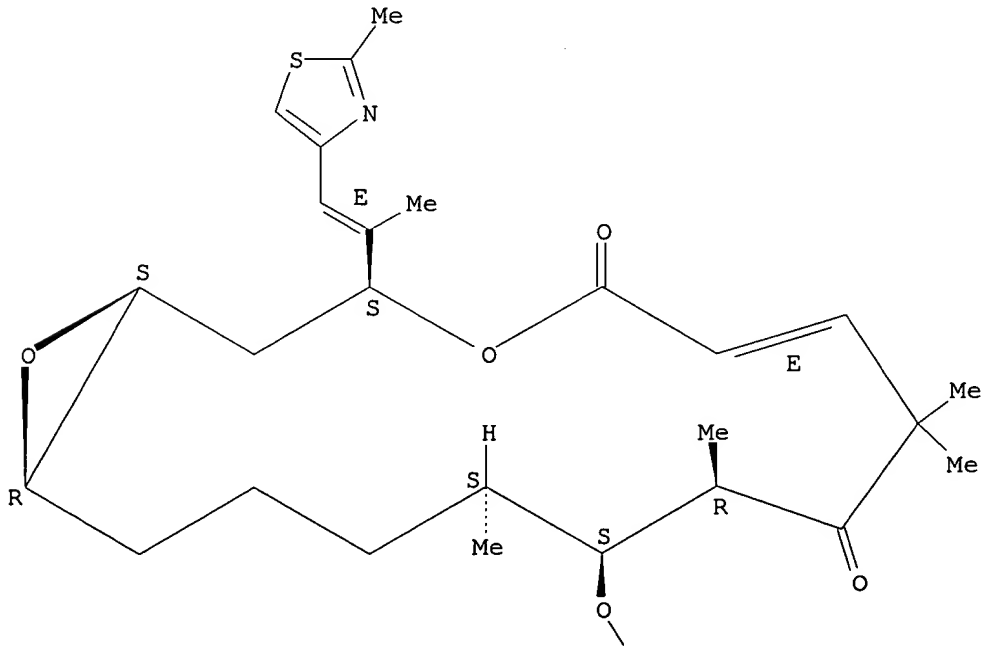
Relative stereochemistry.
Double bond geometry as shown.



RN 191105-89-2 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-(formyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

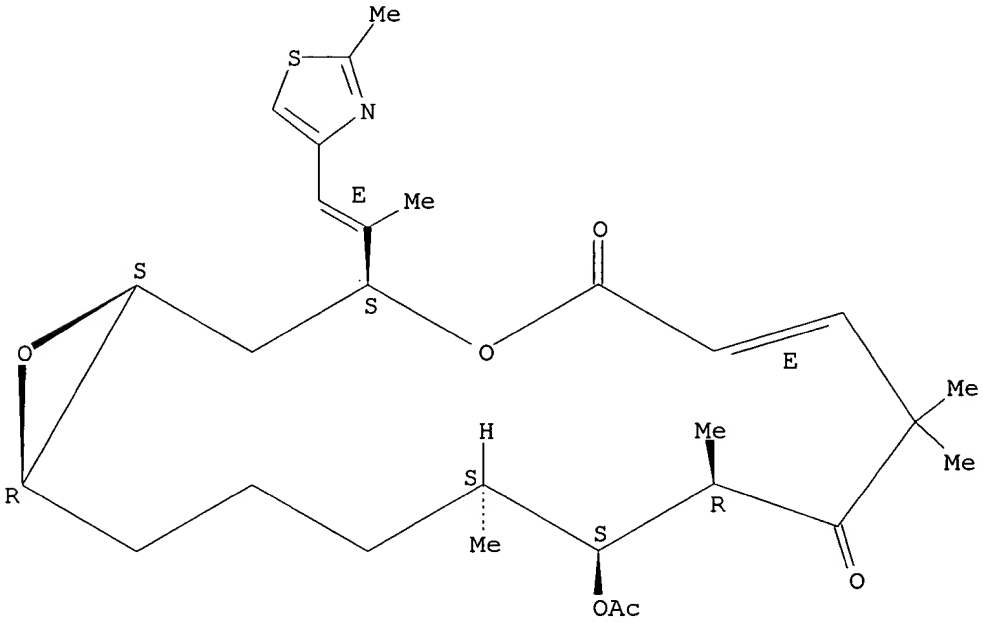
Relative stereochemistry.
Double bond geometry as shown.

PAGE 1-A



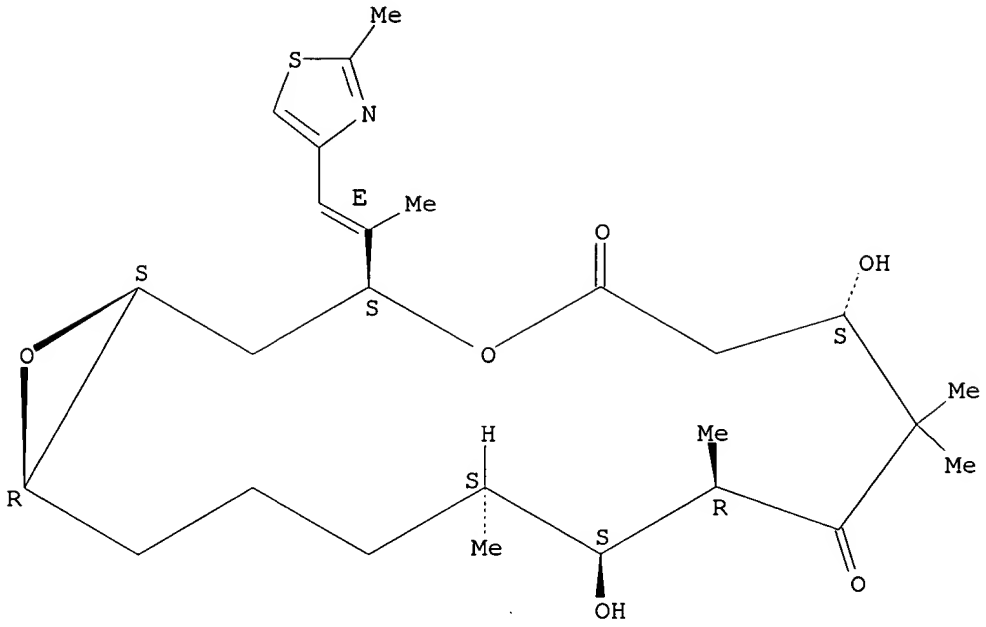
RN 191105-90-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-(acetyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



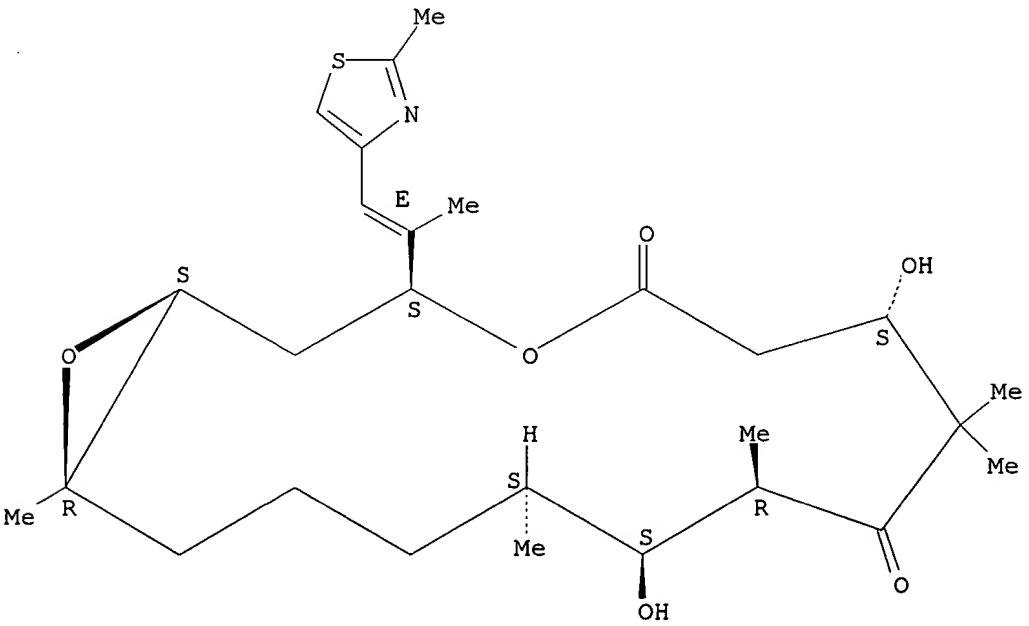
IT **152044-53-6**, Epothilone A **152044-54-7**, Epothilone B **191105-93-8 191105-94-9 191105-95-0**
RL: RCT (Reactant)
(prepn. of epothilone derivs. as agrochems. and pharmaceuticals)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

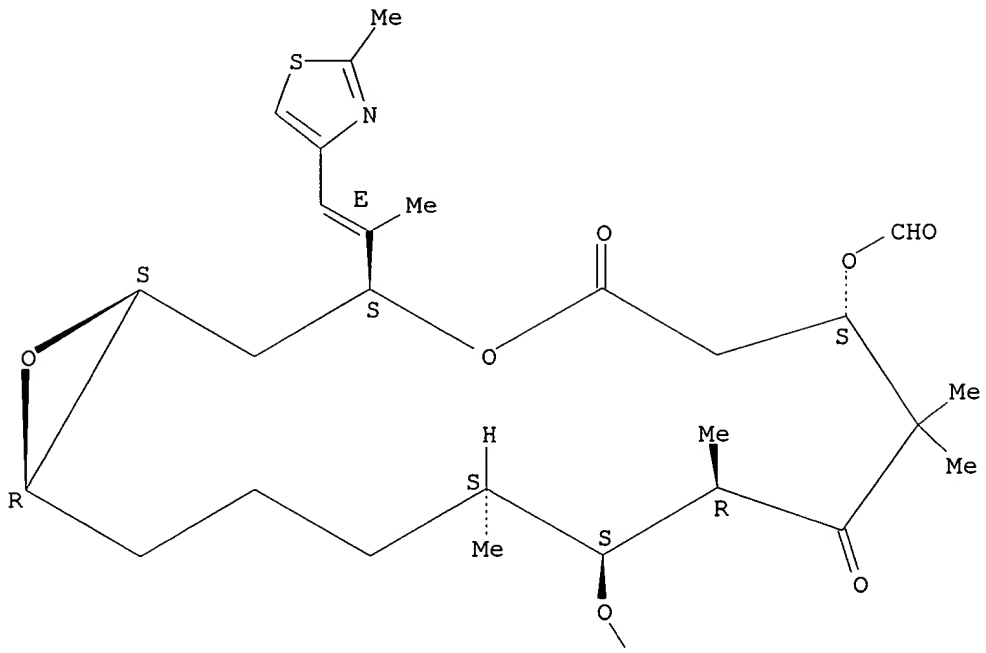
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 191105-93-8 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-bis(formyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

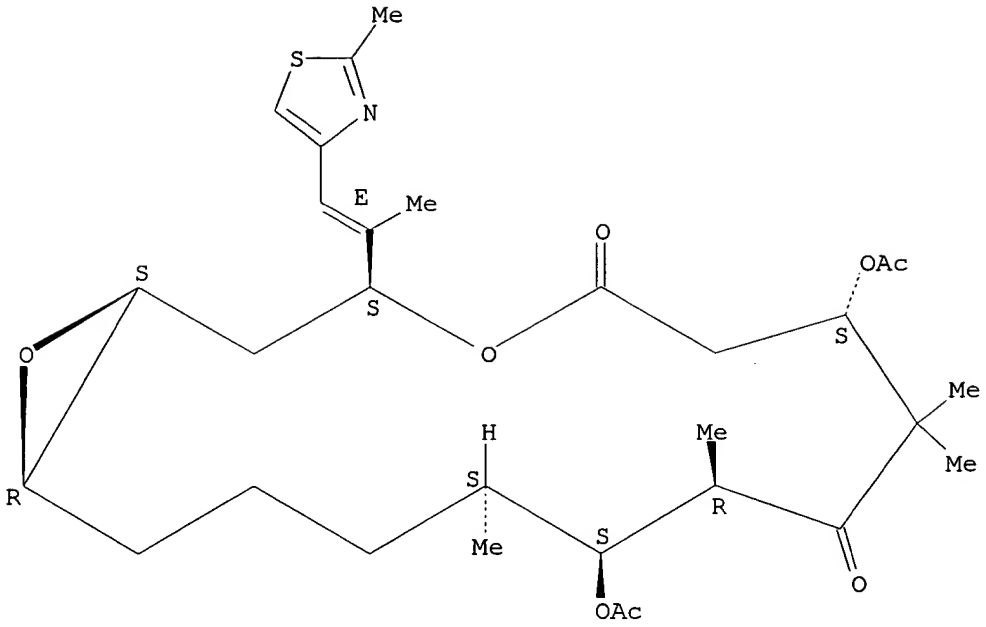
PAGE 1-A



PAGE 2-A

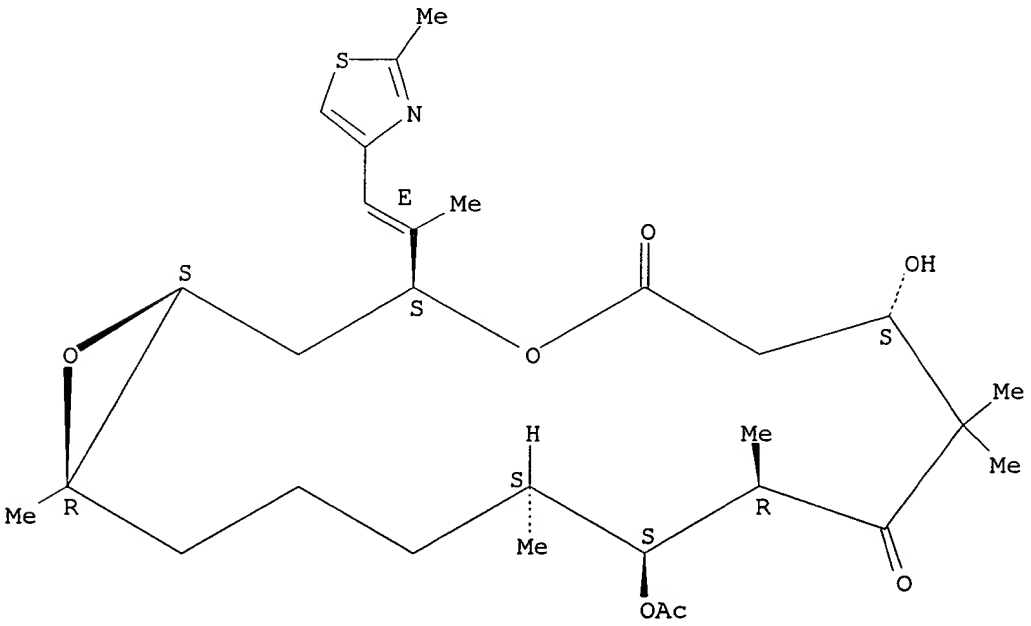
RN 191105-94-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-bis(acetyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 191105-95-0 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 11-(acetyloxy)-7-hydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

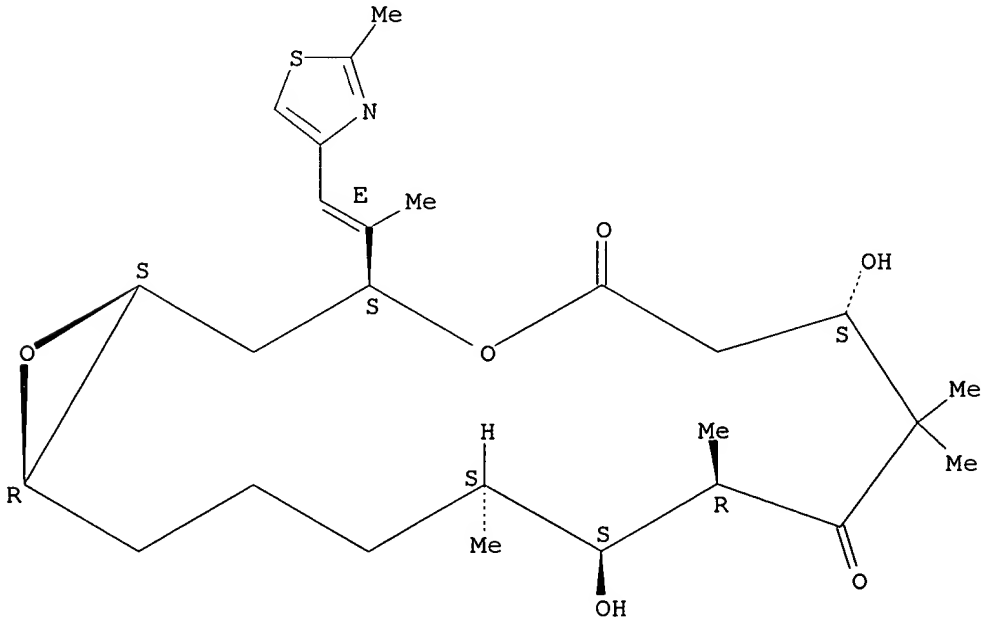
Relative stereochemistry.
Double bond geometry as shown.



L4 ANSWER 182 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:455072 CAPLUS
DN 127:156078

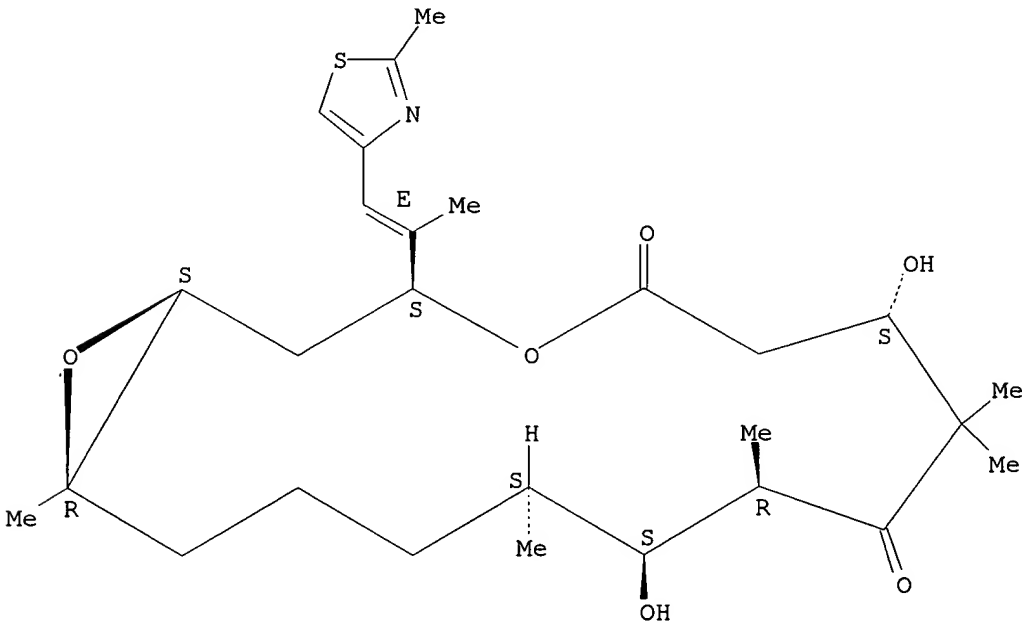
TI Epothilones: novel microtubule-stabilizing agents
AU Bollag, Daniel M.
CS Merck Res. Lab., West Point, PA, 19486, USA
SO Expert Opin. Invest. Drugs (1997), 6(7), 867-873
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
AB A review with 44 refs. The past few years have witnessed the regulatory approvals of the anticancer microtubule stabilizing taxane drugs, Taxol and Taxotere which are rapidly gaining acceptance as important antineoplastic agents with potential against numerous solid tumor malignancies. Despite a basic understanding of the biochem. target of taxanes dating back nearly 20 yr, new classes of tubulin-binding microtubule polymn. enhancers were only reported in the last two years. Epothilones and discodermolide are newly discovered compds., which are structurally distinct from the taxanes, but which possess similar tubulin polymg. and cell biol. effects. In the first studies reported, these compds. displayed similar or greater potencies than taxanes, and the epothilones may represent an advance over the taxanes in retaining toxicity against various taxane-resistant cell lines. This review summarizes the data published on epothilones and discodermolide and proposes further steps that could establish these new classes of compds. as potential second generation microtubule polymn. enhancers.
IT **152044-53-6**, Epothilone A **152044-54-7**, Epothilone B
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epothilones and discodermolide as novel microtubule-stabilizing agents in relation to anticancer activity in humans and lab. animals)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



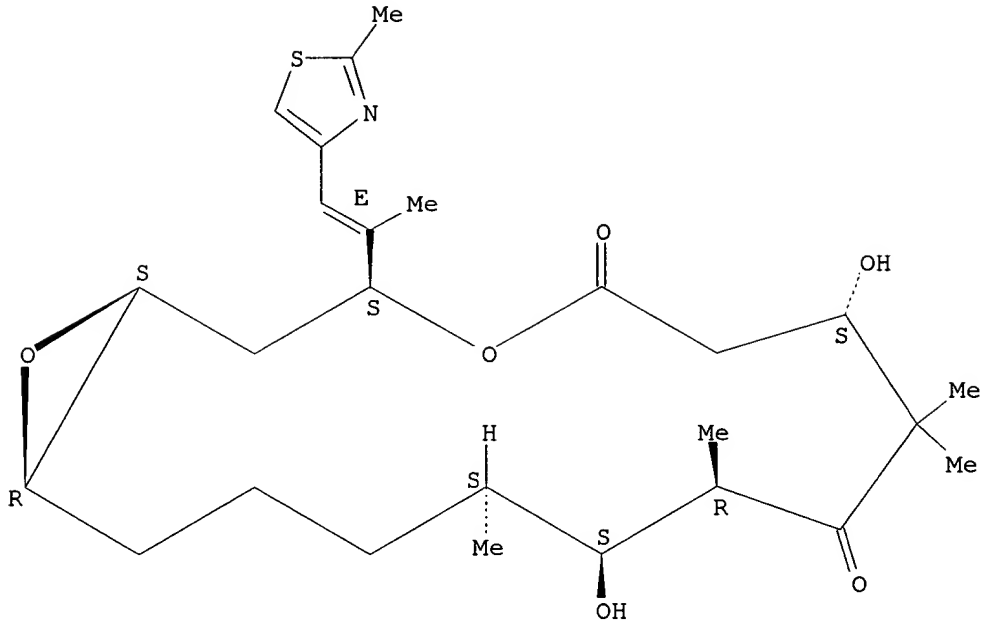
RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 183 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:447517 CAPLUS
DN 127:121574
TI Total synthesis of antitumor antibiotic epothilone having same action mechanism with taxol
AU Nakamura, Seiichi; Hashimoto, Shunichi
CS Yakugakubu, Hokkaido Daigaku, Sapporo, 060, Japan
SO Kagaku (Kyoto) (1997), 52(7), 70-71
CODEN: KAKYAU; ISSN: 0451-1964
PB Kagaku Dojin
DT Journal; General Review
LA Japanese
AB A review with 13 refs. on the total synthesis of epothilone A by using aldol reaction, olefin metathesis, or macrolactonization.
IT **152044-53-6P**, Epothilone A
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of antitumor antibiotic epothilone having same action mechanism with taxol)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

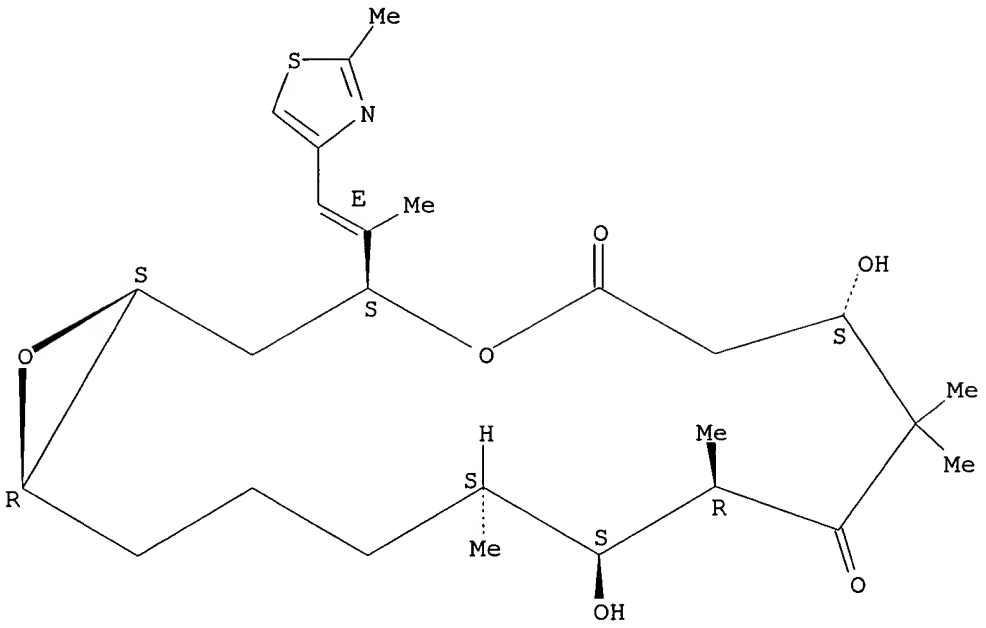
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 184 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:445231 CAPLUS
DN 127:117170
TI Epothilone A induces apoptosis in neuroblastoma cells with multiple mechanisms of drug resistance
AU Wolff, Armin; Technau, Antje; Brandner, Gerhard
CS Abteilung Virologie, Institut fur Medizinische Mikrobiologie und Hygiene der Universitat, Freiburg, D-79008, Germany
SO Int. J. Oncol. (1997), 11(1), 123-126
CODEN: IJONES; ISSN: 1019-6439
PB International Journal of Oncology
DT Journal
LA English
AB Epothilone A, a novel macrolide antibiotic, is produced by the myxobacterium Sorangium cellulosum. Similarly to paclitaxel (Taxol), epothilone A inhibits cell proliferation and induces apoptosis by binding to tubulin and stabilizing of microtubuli. Like paclitaxel, epothilone A induced apoptosis in neuroblastoma cells which exhibit constitutive cytoplasmic sequestration of p53 and, hence, an impaired DNA-damage-dependent apoptosis. However, in contrast to paclitaxel, epothilone A was also effective against a constitutively Pgp-expressing, multidrug resistant neuroblastoma cell line (SK-N-SH). Moreover, the efficacy of epothilone A was not impaired even though the Pgp level was further increased during treatment with the drug.
IT **152044-53-6**, Epothilone A
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of epothilone A in multidrug resistant neuroblastoma cells)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

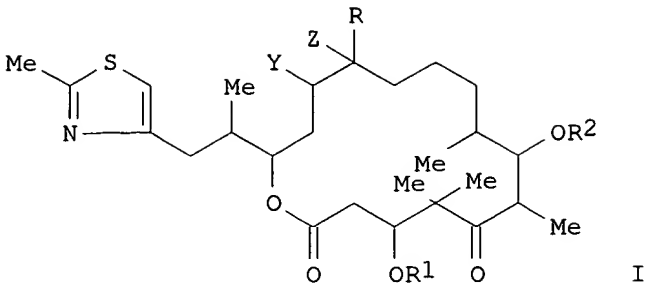
Double bond geometry as shown.



L4 ANSWER 185 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:443365 CAPLUS
DN 127:81289
TI Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
IN Hofle, Gerhard; Kiffe, Michael
PA Gesellschaft Fur Biotechnologische Forschung Mbh (Gbf), Germany; Hofle, Gerhard; Kiffe, Michael
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9719086	A1	19970529	WO 1996-EP5080	19961118
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19542986	A1	19970522	DE 1995-19542986	19951117
	DE 19639456	A1	19980326	DE 1996-19639456	19960925
	EP 873341	A1	19981028	EP 1996-939097	19961118
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000500757	T2	20000125	JP 1997-519381	19961118
PRAI	DE 1995-19542986		19951117		
	DE 1996-19639456		19960925		
	WO 1996-EP5080		19961118		

OS MARPAT 127:81289
GI



I

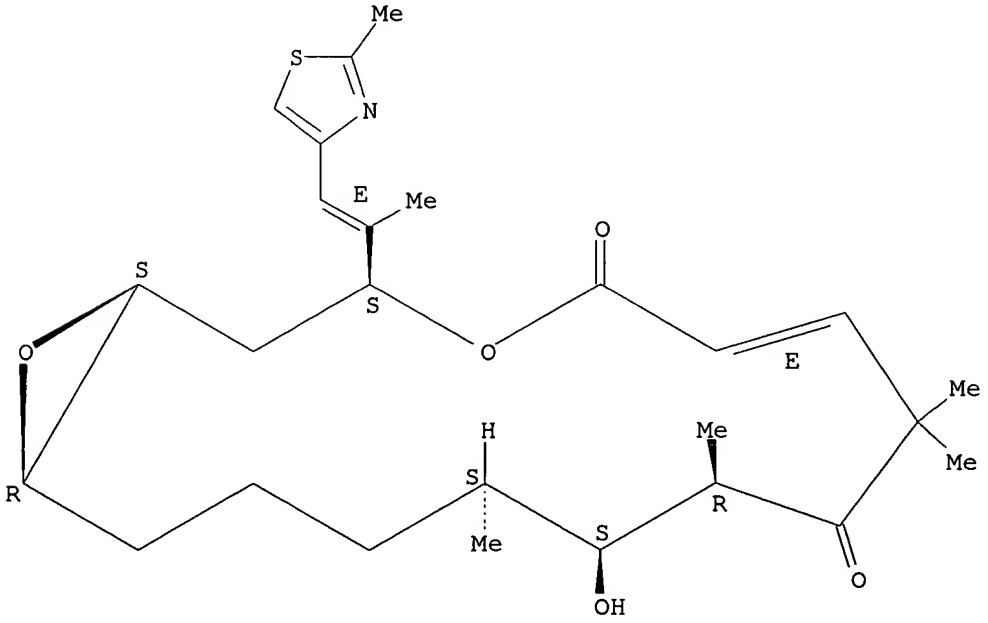
AB The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = H, halo, pseudohalo, OH, acyloxy, alkoxy, benzoyloxy; or YZ = O, bond; however, I may not be epothilone A or B] , useful as agrochems. and pharmaceuticals (no data), are prepd. Thus, epothilone A in acetone contg. trifluoroacetic acid was heated overnight at 50.degree. and the reaction mixt. was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT **191105-88-1P 191105-89-2P 191105-90-5P**
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone derivs. as agrochems. and pharmaceuticals)

RN 191105-88-1 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



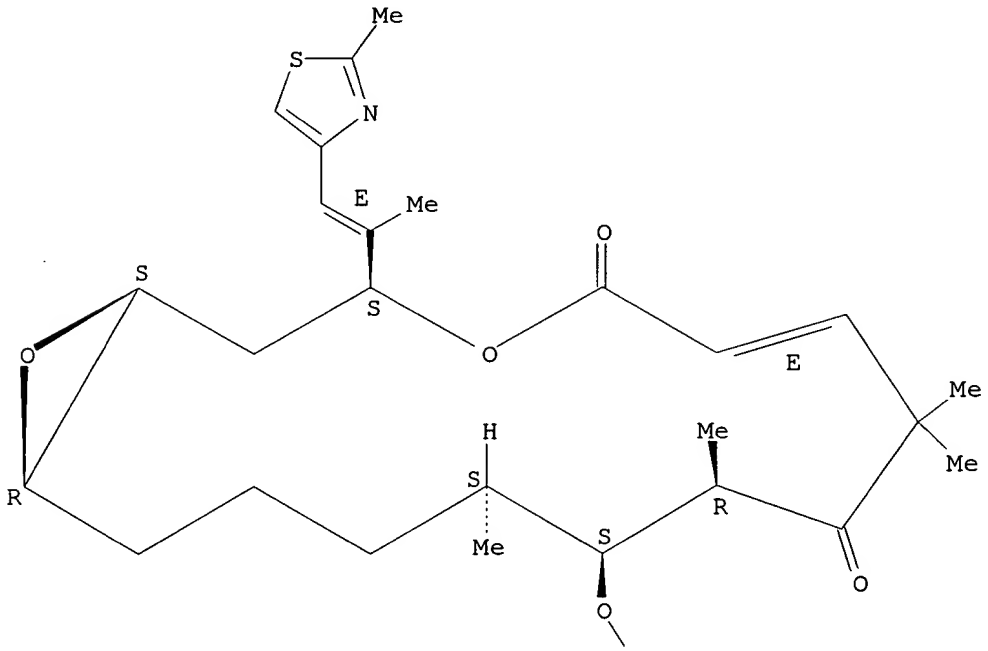
RN 191105-89-2 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-(formyloxy)-

8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
[1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

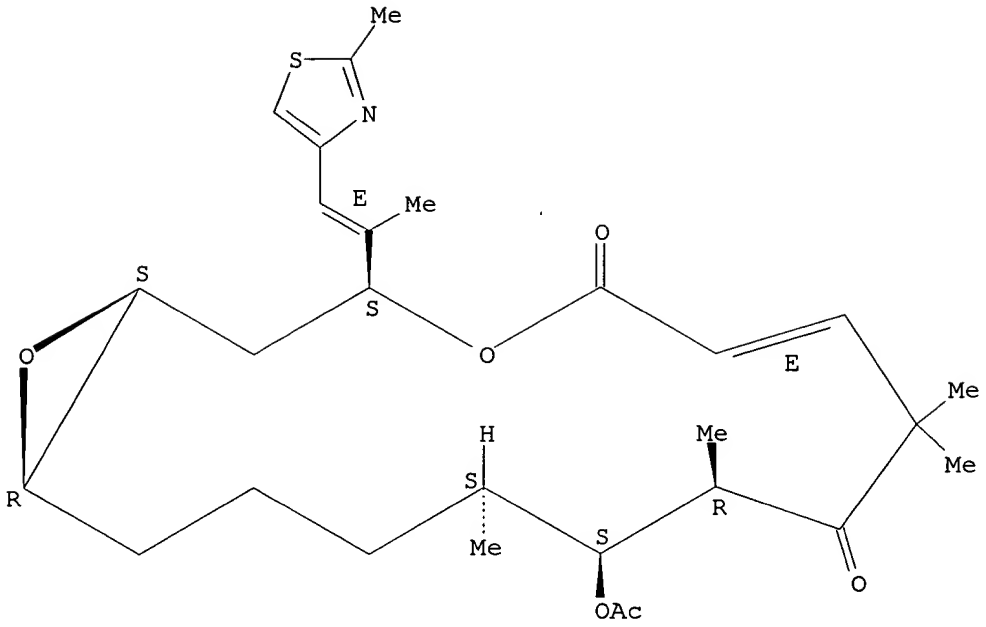
PAGE 1-A



PAGE 2-A

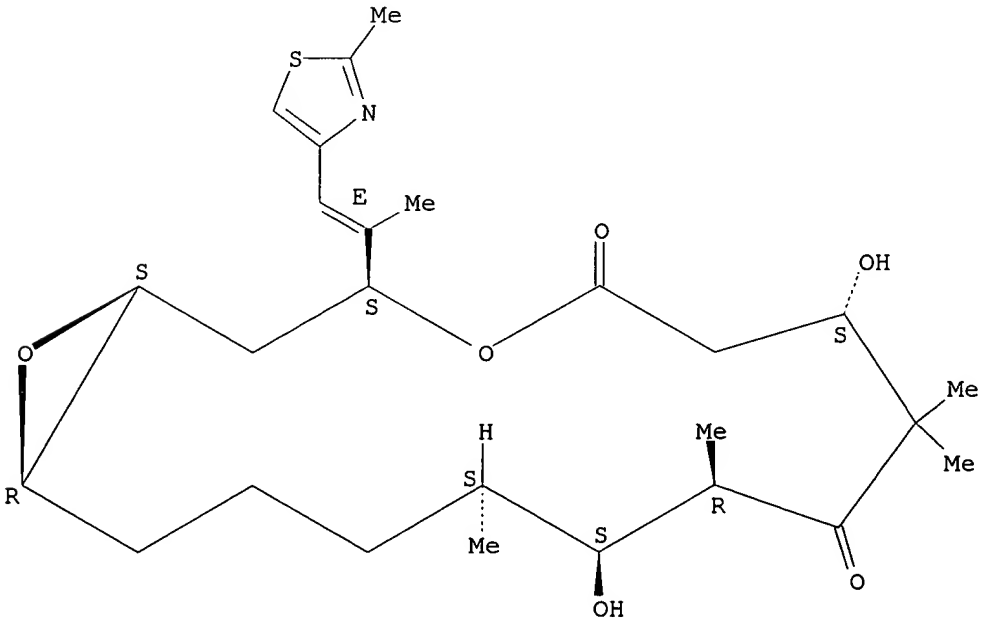
RN 191105-90-5 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadec-6-ene-5,9-dione, 11-(acetyloxy)-
8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-,
[1R*,3R*(E),6E,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



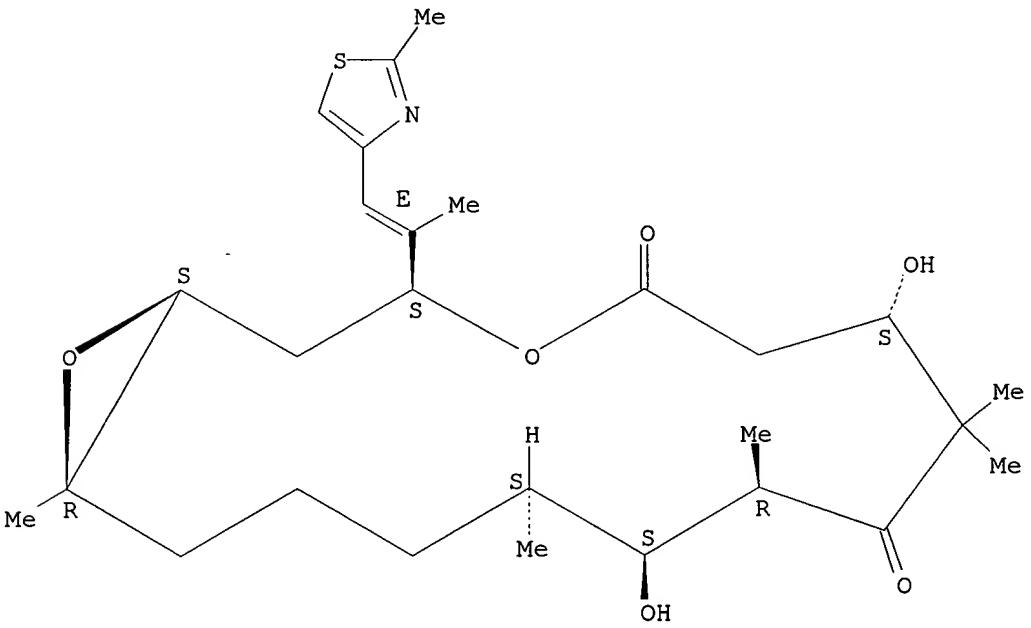
IT **152044-53-6**, Epothilone A **152044-54-7**, Epothilone B
191105-93-8 191105-94-9 191105-95-0
RL: RCT (Reactant)
(prepn. of epothilone derivs. as agrochems. and pharmaceuticals)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

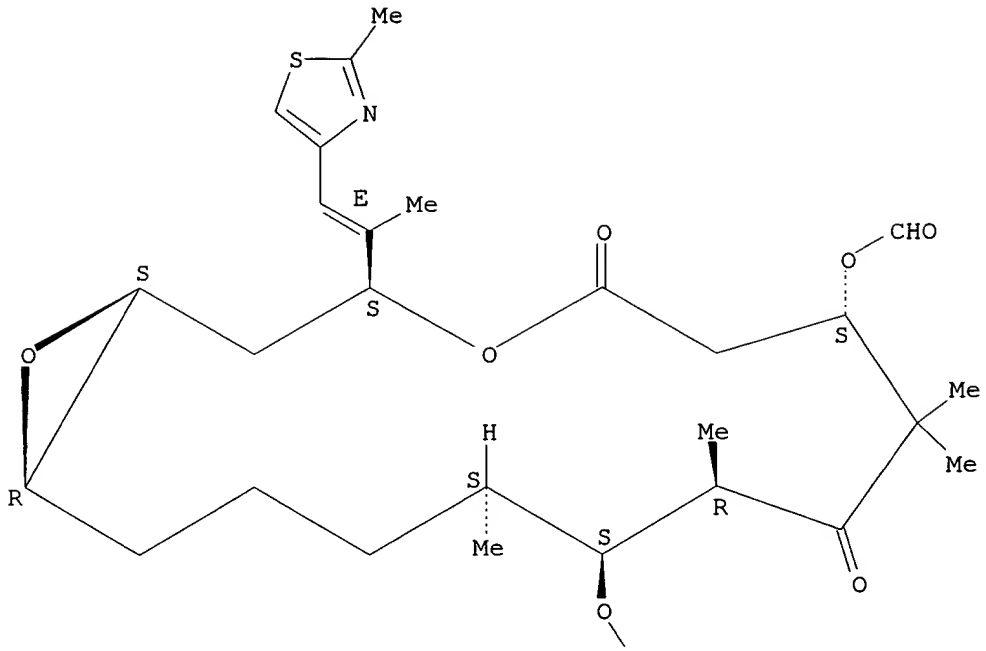
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 191105-93-8 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-bis(formyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

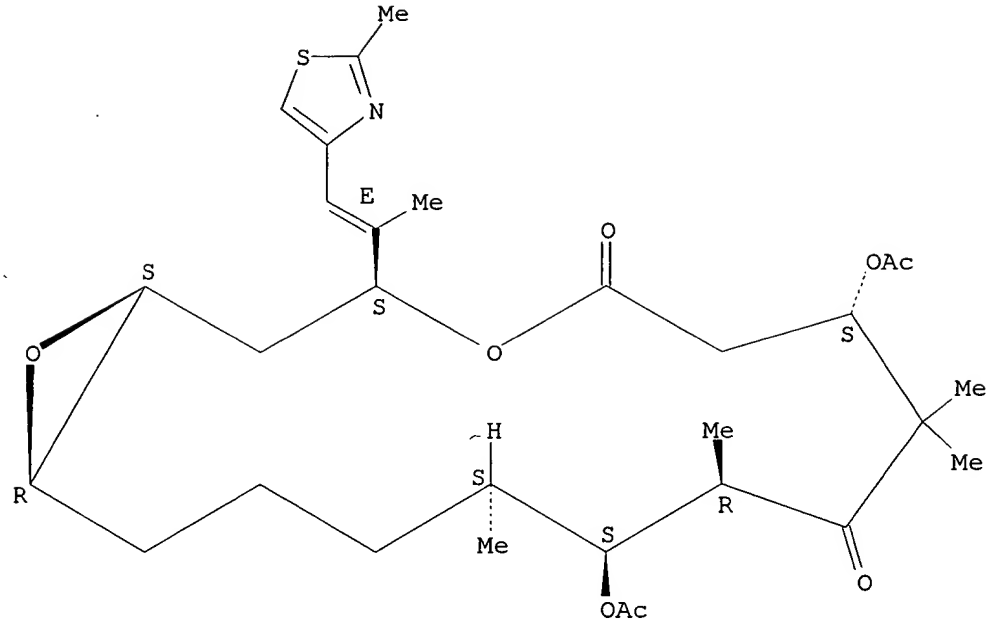
PAGE 1-A



PAGE 2-A

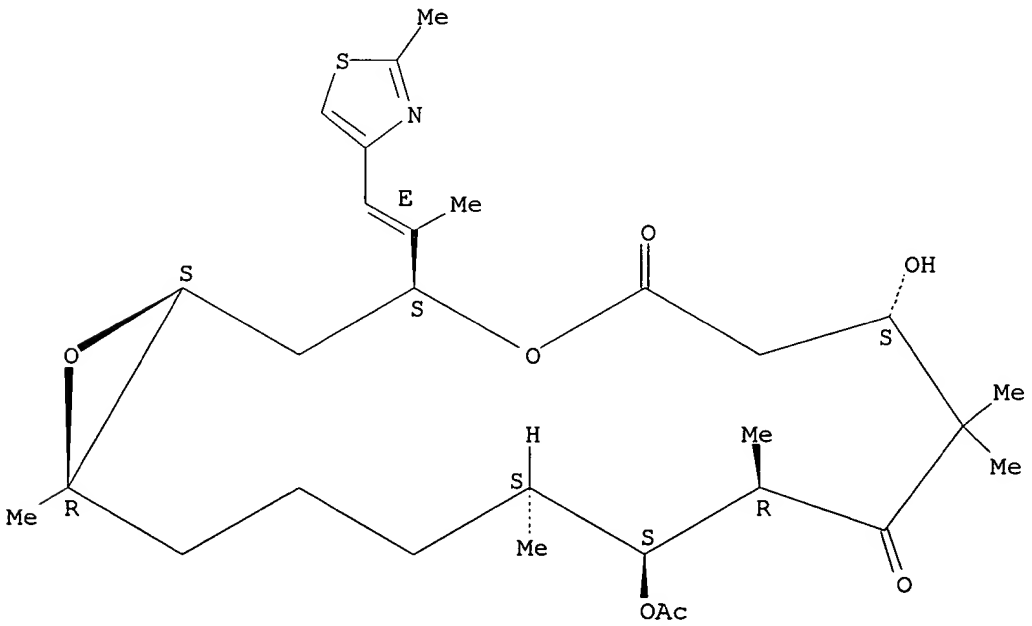
RN 191105-94-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-bis(acetyloxy)-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 191105-95-0 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 11-(acetyloxy)-7-hydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L4 ANSWER 186 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:430309 CAPLUS
DN 127:108793

TI Stereoselective syntheses and evaluation of compounds in the 8-desmethylepothilone A series: some surprising observations regarding their chemical and biological properties

AU Balog, Aaron; Betinato, Peter; Su, Dai-Shi; Meng, Dongfang; Sorensen, Erik; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.

CS Lab. Bioorganic Chem., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA

SO Tetrahedron Lett. (1997), 38(26), 4529-4532
CODEN: TELEAY; ISSN: 0040-4039

PB Elsevier

DT Journal

LA English

OS CASREACT 127:108793

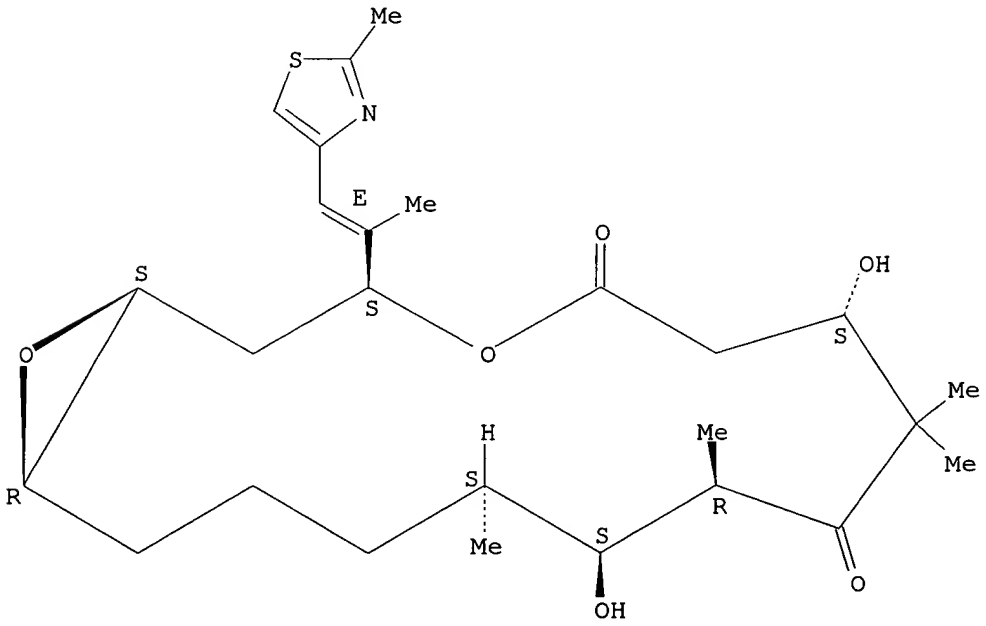
AB The title compds. have been synthesized in a convergent way by recourse to a Weiler type dianion construction.

IT **152044-53-6**, Epothilone A **152044-54-7**, Epothilone B
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(stereoselective syntheses and evaluation of compds. in the 8-desmethylepothilone A series)

RN 152044-53-6 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

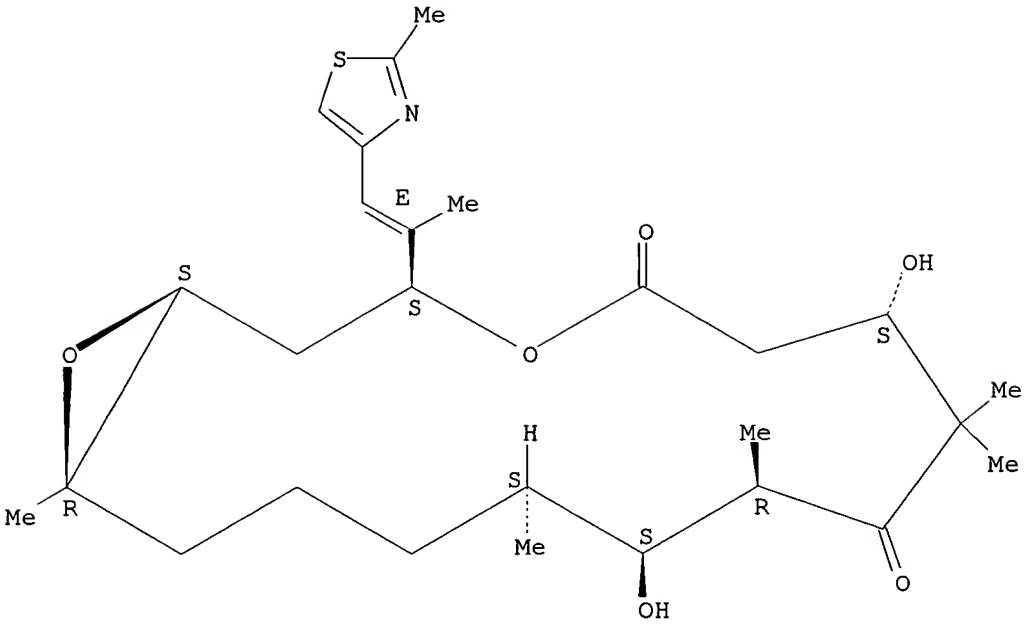
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



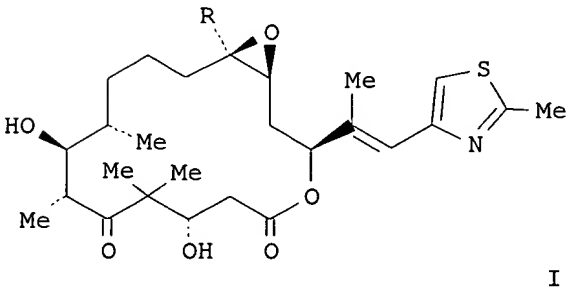
RN 152044-54-7 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 187 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:330310 CAPLUS
DN 127:4950
TI Synthesis of epothilones A and B in solid and solution phase
AU Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CS Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Nature (London) (1997), 387(6630), 268-272
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
OS CASREACT 127:4950
GI



I

AB Epothilones A (I; R = H) and B (I: R = Me), two compds. that were recently isolated from myxobacterium Sorangium cellulosum strain 90, have generated intense interest among chemists, biologists and clinicians owing to the structural complexity, unusual mechanism of interaction with microtubules and anticancer potential of these mols. Like taxol, they exhibit cytotoxicity against tumor cells by inducing microtubule assembly and

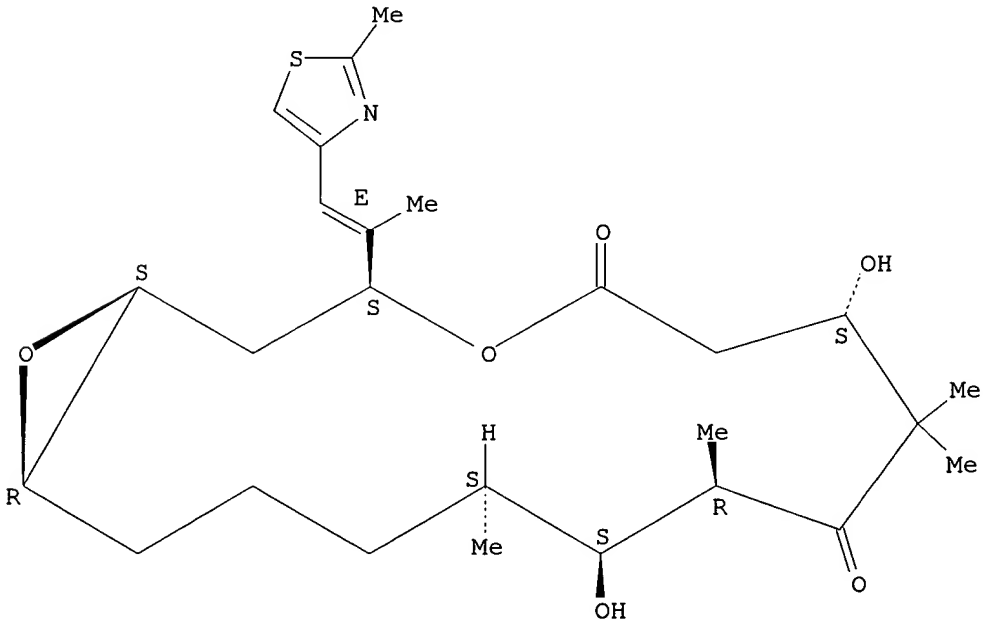
stabilization, even in taxol-resistant cell lines. Following the structural elucidation of these mols. by X-ray crystallog. in 1996, several synthesis of epothilones A and B have been reported, indicative of the potential importance of these mols. in the cancer field. Here we report the first solid-phase synthesis of epothilone A, the total synthesis of epothilone B, and the generation of a small epothilone library. The solid-phase synthesis applied here to epothilone A could open up new possibilities in natural-product synthesis and, together with soln.-phase synthesis of other epothilones, paves the way for the generation of large combinatorial libraries of these important mols. for biol. screening.

IT **152044-53-6P**, Epothilone A **152044-54-7P**, Epothilone B
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of epothilone A and soln.-phase synthesis of epothilone B)

RN 152044-53-6 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

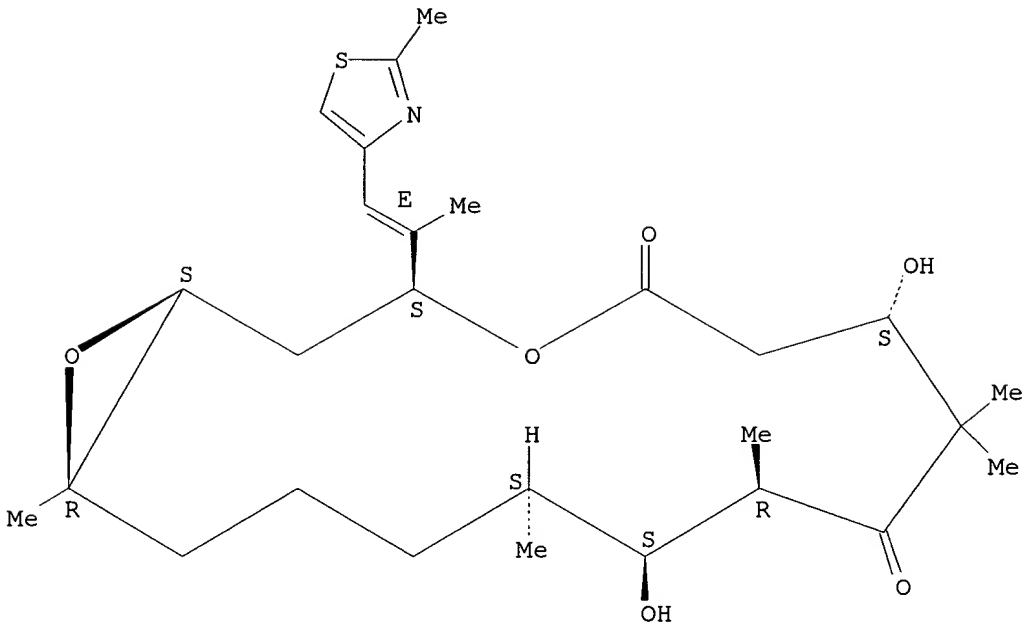
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 152044-54-7 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

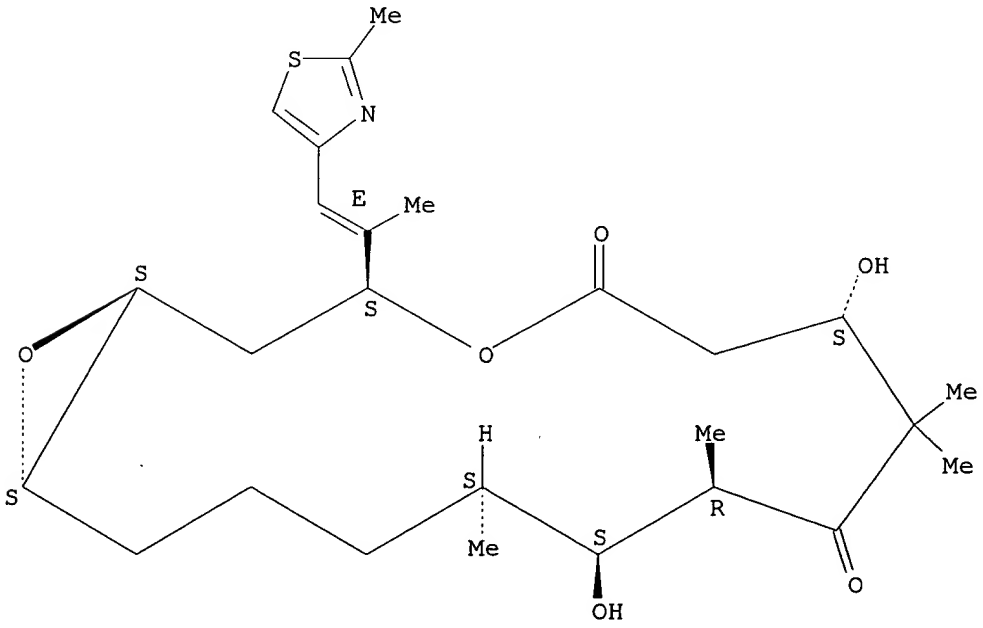


IT **190369-91-6P 190370-10-6P 190370-11-7P 190370-13-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library via solid-phase synthesis of epothilone A and soln.-phase synthesis of epothilone B)

RN 190369-91-6 CAPLUS

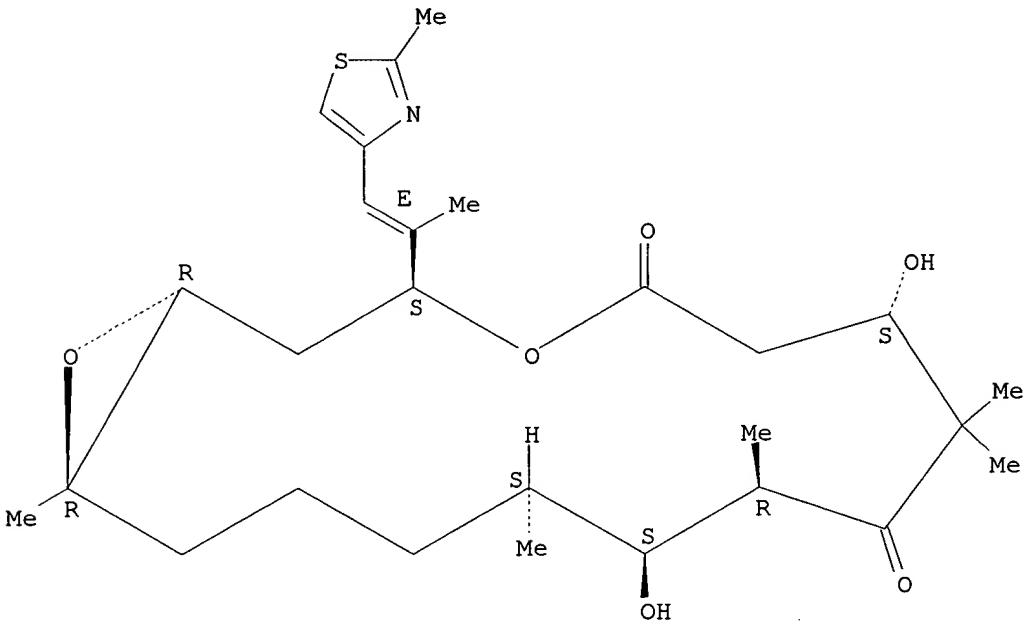
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



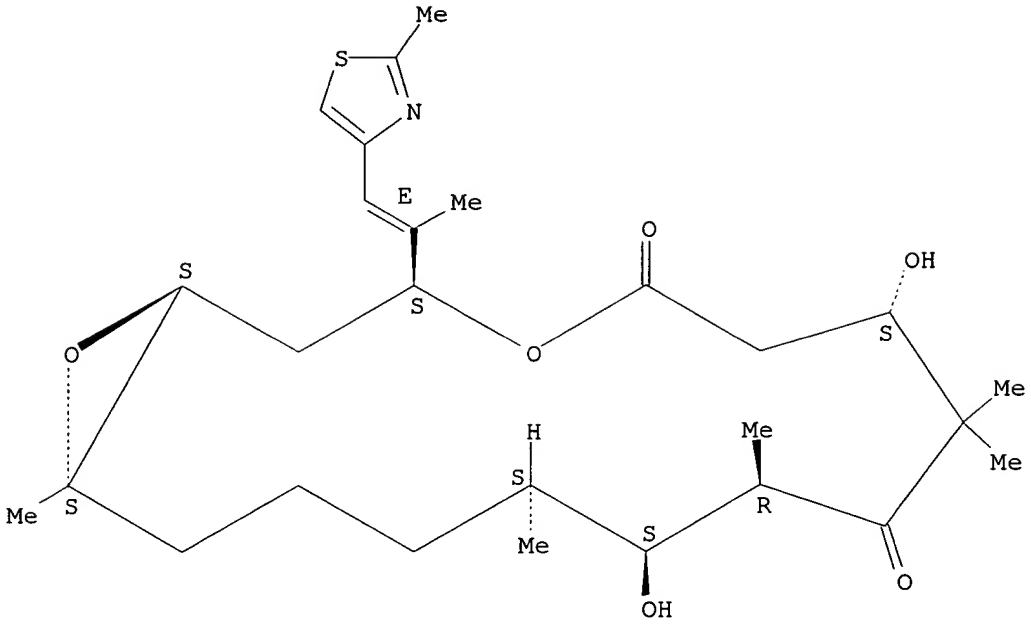
RN 190370-10-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



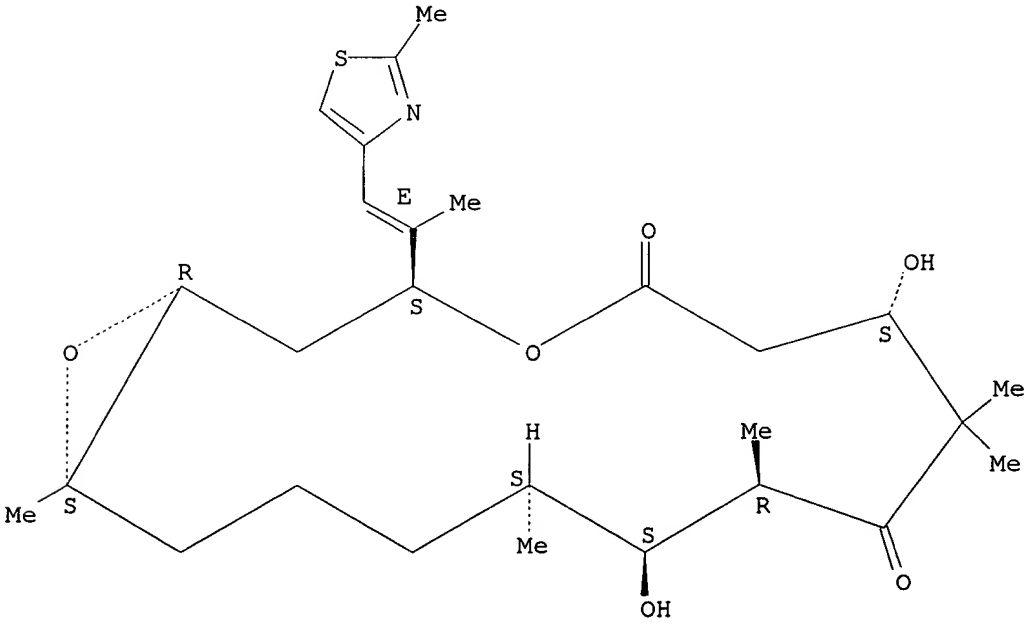
RN 190370-11-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190370-13-9 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1R,3S,7S,10R,11S,12S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 188 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:302059 CAPLUS
DN 127:4948

TI Total synthesis of (-)-epothilone B: an extension of the Suzuki coupling method and insights into structure-activity relationships of the epothilones

AU Su, Dai-Shi; Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.

CS Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA

SO Angew. Chem., Int. Ed. Engl. (1997), 36(7), 757-759
CODEN: ACIEAY; ISSN: 0570-0833

PB VCH

DT Journal

LA English

OS CASREACT 127:4948

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

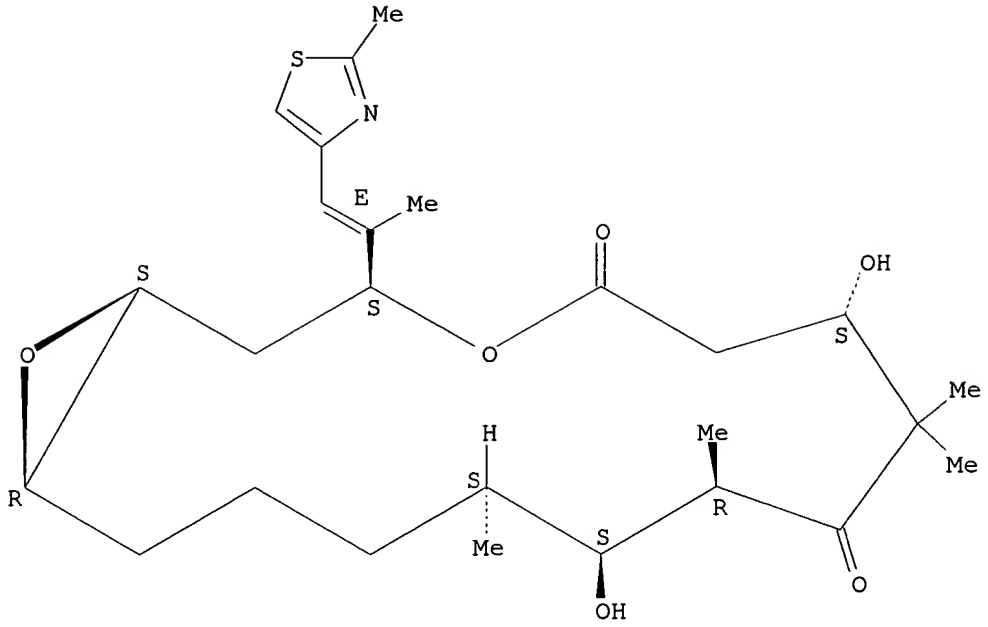
AB (-)-Epothilone B (I; R = Me, X = O) and desoxyepothilone B (I; R = Me, X = bond) were prepd. via Suzuki coupling of (Z)-vinyl iodide II with borane III. I (R = H, Me, X = O, bond) and the E-isomers of I (R = H, Me, X = bond) were tested for efficacy against drug-sensitive and resistant CCRF-CEM cell lines (IC50 = 0.0004 - 0.262 .mu.M).

IT **152044-53-6**, Epothilone A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)

RN 152044-53-6 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

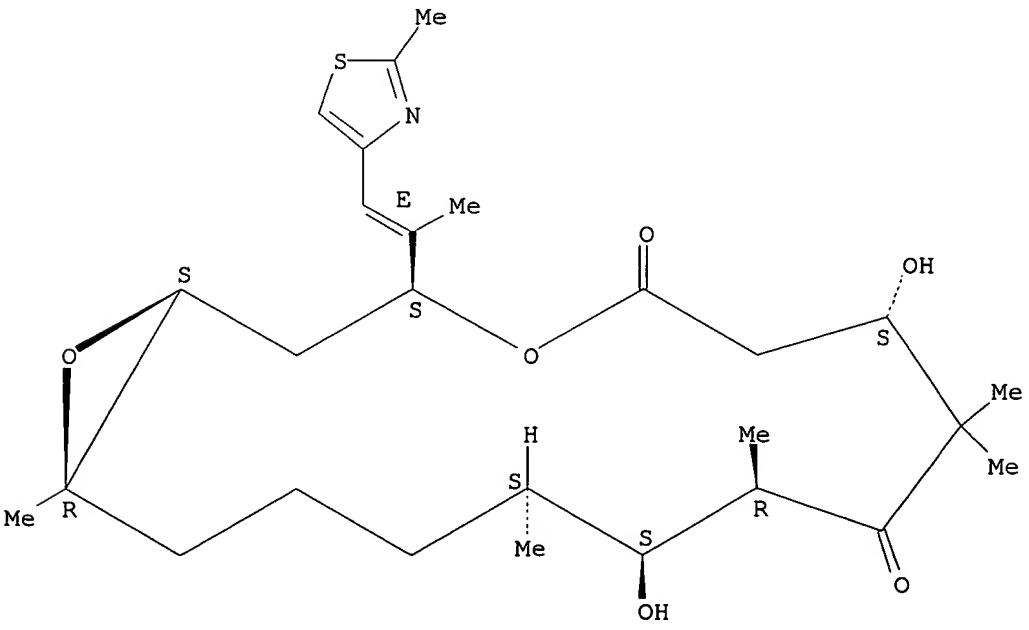


IT **152044-54-7P**, (-)-Epothilone B
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)

RN 152044-54-7 CAPLUS

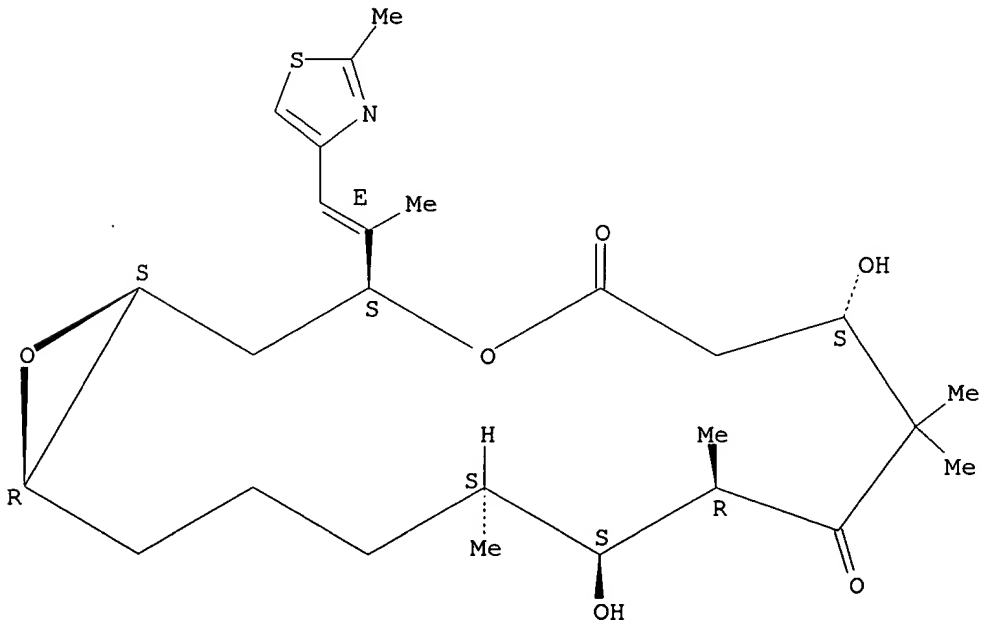
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



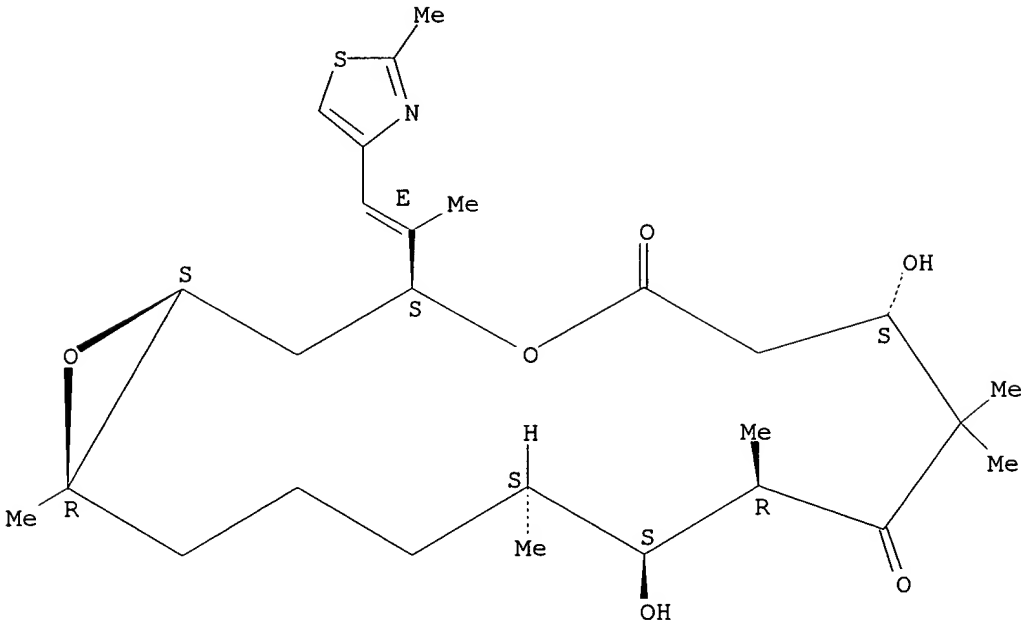
L4 ANSWER 189 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:216288 CAPLUS
DN 126:251012
TI Towards the synthesis of epothilone A: enantioselective preparation of the thiazole sidechain and macrocyclic ring closure
AU Taylor, Richard E.; Haley, Jeffrey D.
CS Dep. Chemistry and Biochemistry, Univ. Notre Dame, Notre Dame, IN, 46556, USA
SO Tetrahedron Lett. (1997), 38(12), 2061-2064
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 126:251012
AB A synthetic approach to a new class of microtubule-stabilizing natural products is described which employs a macrocyclic olefination strategy to cyclize the 16-membered lactone ring. The C(13)-C(19) thiazole subunit of epothilone A and B is prepd. in high enantioselectivity using a catalytic asym. allylation reaction.
IT **152044-53-6P**, Epothilone A **152044-54-7P**, Epothilone B
RL: PNU (Preparation, unclassified); PREP (Preparation)
(stereoselective prepn. of the thiazole fragment of epothilone A and B)
RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

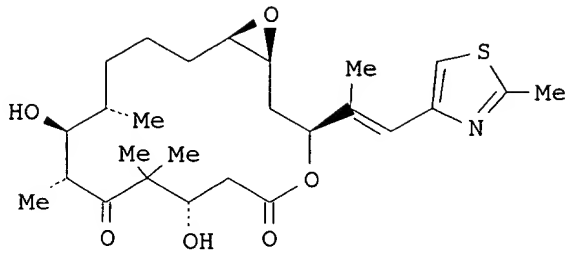


RN 152044-54-7 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

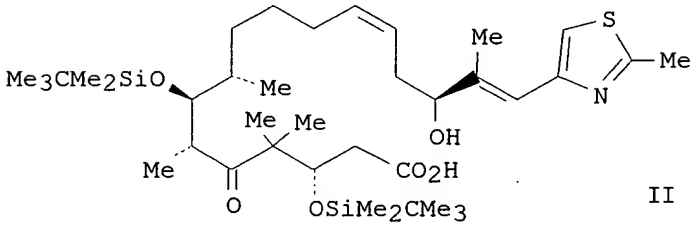
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 190 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:206419 CAPLUS
DN 126:251010
TI Total synthesis of epothilone A: the macrolactonization approach
AU Nicolaou, K. C.; Sarabia, Francisco; Ninkovic, Sacha; Yang, Zhen
CS Dep. Chem., Skaggs Inst. Chem. Biol. Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Angew. Chem., Int. Ed. Engl. (1997), 36(5), 525-527
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:251010
GI



I



II

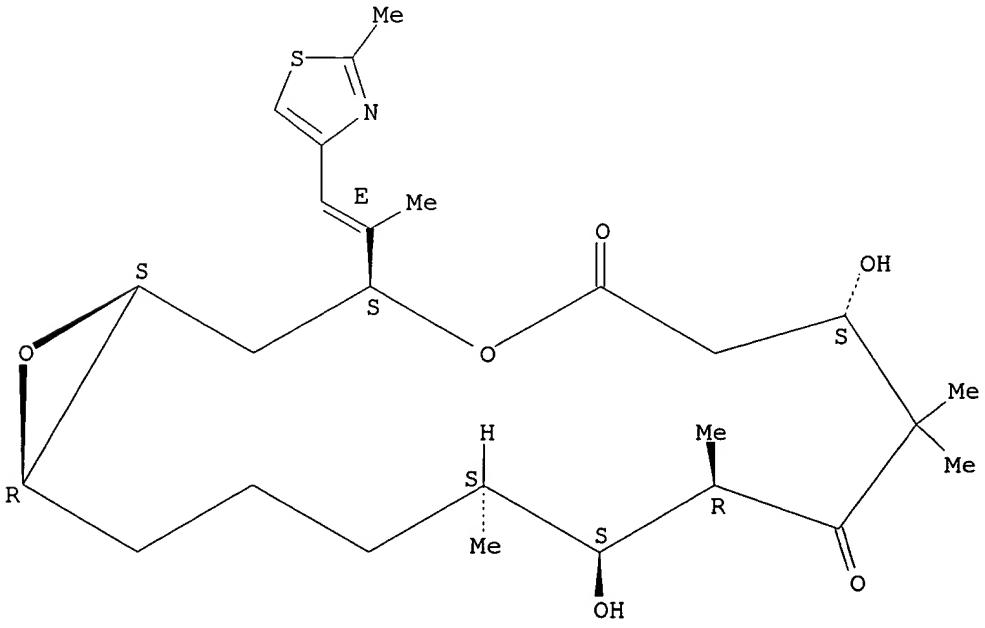
AB Epothilone A (I) was prepd. via a highly convergent and flexible route with macrolactonization of hydroxy acid II as the key step.

IT **152044-53-6P,** Epothilone A
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of epothilone A via a macrolactonization approach)

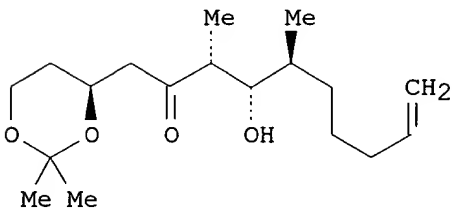
RN 152044-53-6 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

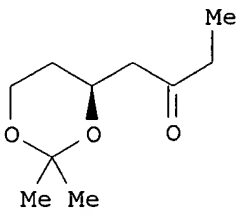
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 191 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:206418 CAPLUS
DN 126:277316
TI Total synthesis of (-)-epothilone A
AU Schinzer, Dieter; Limberg, Anja; Bauer, Armin; Boehm, Oliver M.; Cordes, Martin
CS Dip. Chim., Inst. Org. Chem. Tech. Univ. Hagenring, Braunschweig, D-38106, Germany
SO Angew. Chem., Int. Ed. Engl. (1997), 36(5), 523-524
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 126:277316
GI



I



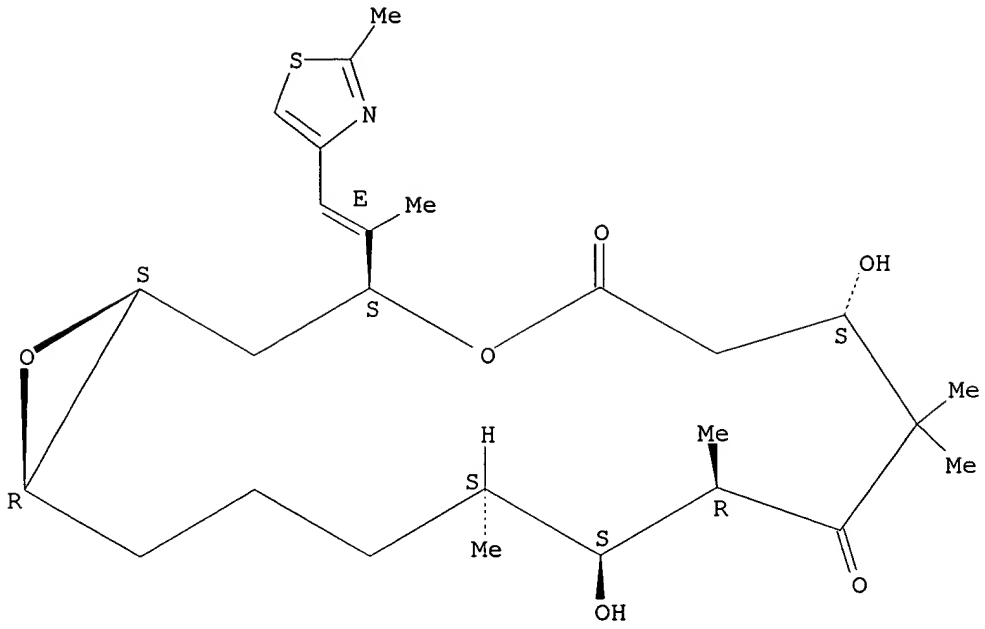
II

AB Stereoselective total synthesis of (-)-epothilone A and epothilone C was reported. The key step was the diastereoselective prepn. of intermediate ketone I by an aldol condensation of II with (S)-2-methyl-6-heptenal.

IT **152044-53-6P**, (-)-Epothilone A
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-epothilone A)

RN 152044-53-6 CAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 192 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:175662 CAPLUS
DN 126:225133
TI Remote Effects in Macrolide Formation through Ring-Forming Olefin Metathesis: An Application to the Synthesis of Fully Active Epothilone Congeners
AU Meng, Dongfang; Su, Dai-Shi; Balog, Aaron; Bertinato, Peter; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CS Laboratories for Bioorganic Chemistry and Biochemical Pharmacology, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SO J. Am. Chem. Soc. (1997), 119(11), 2733-2734
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 126:225133
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A ring closing olefin metathesis strategy for the synthesis of the previously encountered desoxyepothilone A (I) is described. A merging of the alkyl segment II (carbons 12-21) and acyl segment III (carbons 3-11) through an intermol. aldol-condensation reaction provided substrates needed for ring closing olefin metathesis. Thus, thiazole IV underwent olefin metathesis in C6H6 contg. 50 mol % (PhCH:)[P(cyclohexyl)3]2RuCl2 to give 65% II and its E-isomer (Z:E 1:2). The results of these cyclization indicate a remarkable sensitivity to permutations of functionality at centers remote from the site of olefin metathesis. The in vitro biol. activity of E and Z desoxyepothilone as well as several related congeners is also described. I has IC50 range of 0.012-0.022 .mu.M against

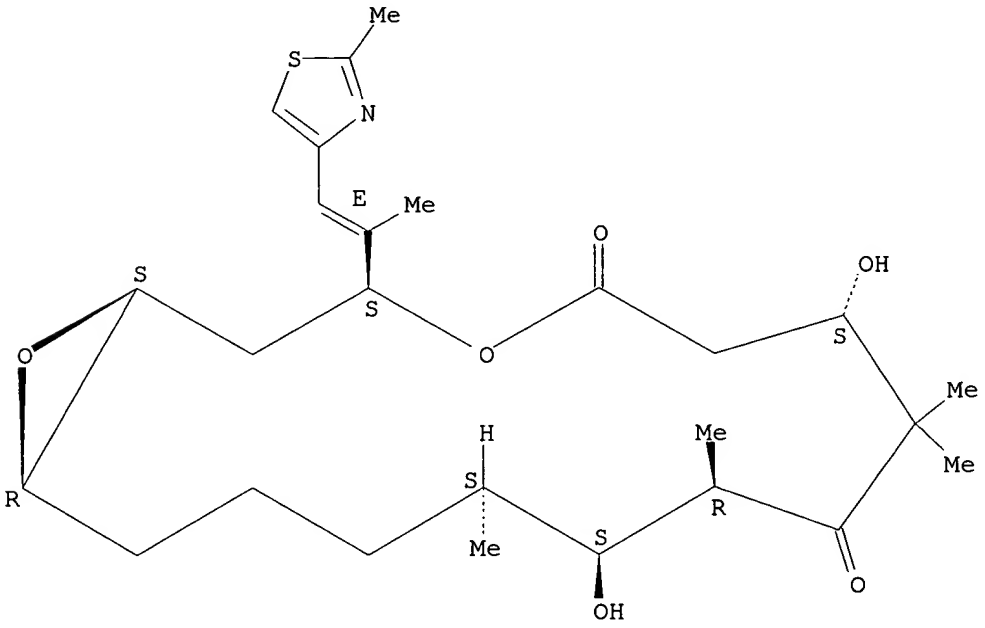
drug-sensitive and -resistant human leukemic CCRF-CEM cell lines.

IT **152044-53-6**, Epothilone A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(prepn. of antitumor epothilone congeners via ring-forming olefin metathesis)

RN 152044-53-6 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7S,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

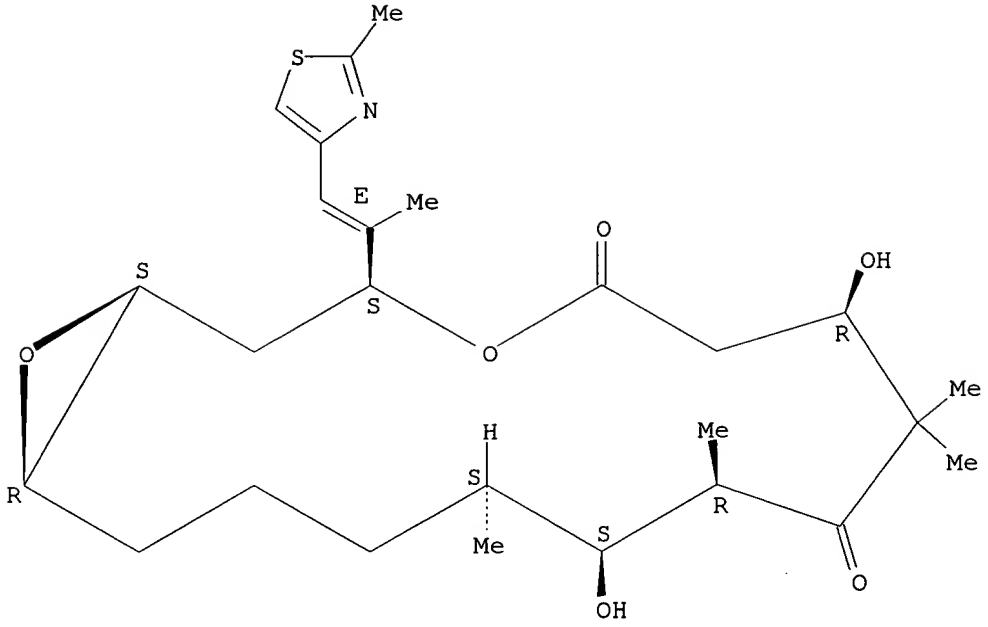


IT **188260-09-5P**, (-)-3-epi-Epothilone A
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of antitumor epothilone congeners via ring-forming olefin metathesis)

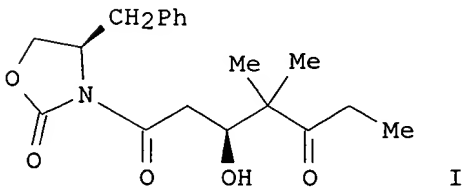
RN 188260-09-5 CAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,7R,10R,11S,12S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L4 ANSWER 193 OF 207 CAPLUS COPYRIGHT 2001 ACS
AN 1997:149902 CAPLUS
DN 126:225130
TI The chromium-Reformatsky reaction: asymmetric synthesis of the aldol fragment of the cytotoxic epothilons from 3-(2-bromoacyl)-2-oxazolidinones
AU Gabriel, Tobias; Wessjohann, Ludger
CS Inst. Org. Chem., Ludwig-Maximilians-Univ. Muenchen, Munich, D-80333, Germany
SO Tetrahedron Lett. (1997), 38(8), 1363-1366
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 126:225130
GI



I

AB In a two step, one pot reaction of 4-benzyloxazolidinone, 2-bromoacetyl halide, chromium dichloride and a suitable 3-oxo-aldehyde deriv. the C1-C6-Me - fragment I of epothilons is available in its correct oxidn. state and enantiomeric form. Compared to common methods, the chromium-Reformatsky variation preferentially yields the opposite diastereomers and gives improved chemo- and diastereoselection.

IT **152044-54-7P**, Epothilone B
RL: PNU (Preparation, unclassified); PREP (Preparation)